
**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**
Washington, D.C. 20549

Form S-1
REGISTRATION STATEMENT
Under
The Securities Act of 1933

PLUS THERAPEUTICS, INC.

(Exact name of Registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

2834
(Primary Standard Industrial
Classification Code Number)

33-0827593
(I.R.S. Employer
Identification Number)

4200 Marathon Blvd., Suite 200
Austin, TX 78756
(737)-255-7194

(Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)

Andrew Sims
Chief Financial Officer
Plus Therapeutics, Inc.
4200 Marathon Blvd., Suite 200
Austin, TX 78756
(737)-255-7194

(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

Andrew L. Strong
William I. Intner
Hogan Lovells US LLP
609 Main Street, Suite 4200
Houston, TX 77002
(713) 632-1400

Approximate date of commencement of proposed sale to the public: From time to time after this registration statement becomes effective, as determined by the selling stockholder.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act, check the following box:

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer
Non-accelerated filer

Accelerated filer
Smaller reporting company
Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with the provisions of Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

**PRELIMINARY PROSPECTUS
(Subject to Completion, Dated November 14, 2023)**

1,300,000 Shares of Common Stock



This prospectus relates to the offer and sale of up to 1,300,000 shares of our common stock, par value \$0.001 per share, by Lincoln Park Capital Fund, LLC, which we refer to in this prospectus as Lincoln Park or the selling stockholder.

The shares of common stock to which this prospectus relates have been and may be issued by us to Lincoln Park pursuant to a purchase agreement, dated as of August 2, 2022, we entered into with Lincoln Park, which we refer to in this prospectus as the Purchase Agreement. We are not selling any securities under this prospectus and will not receive any of the proceeds from the sale of our common stock by the selling stockholder. However, we may receive up to \$50.0 million aggregate gross proceeds from sales of common stock to Lincoln Park under the Purchase Agreement. As of the date of this prospectus, we have received gross proceeds of \$4.2 million from sales of common stock pursuant to the Purchase Agreement, which sales were registered pursuant to two separate registration statements on Form S-1 filed on August 8, 2022, or the 2022 Registration Statement, and August 9, 2023, or the August 2023 Registration Statement. We refer herein to the 2022 Registration Statement and the August 2023 Registration Statement together as the Prior Registration Statements. Of the 2,100,486 shares of our common stock registered for resale pursuant to the Prior Registration Statements, as of as of November 8, 2023, 1,423,319 shares remain available for resale pursuant to the Purchase Agreement under the August 2023 Registration Statement at this time. All share numbers presented in this prospectus reflect the 1-for-15 reverse stock split that we effected on May 1, 2023. Upon execution of the Purchase Agreement, we paid \$125,000 in cash, which we refer to in the prospectus as the Initial Commitment Fee, and issued 32,846 shares of common stock, which we refer to in this prospectus as the Initial Commitment Shares, to Lincoln Park as consideration for its irrevocable commitment to purchase shares of our common stock at our direction under the Purchase Agreement. We have also agreed to pay an additional commitment fee (the "Additional Commitment Fee"), which we may elect to pay in cash and/or shares of our common stock, upon our receipt of \$25.0 million aggregate gross proceeds from sales of common stock to Lincoln Park under the Purchase Agreement. See "The Lincoln Park Transaction" for a description of the Purchase Agreement and "Selling Stockholder" for additional information regarding Lincoln Park.

The selling stockholder may sell or otherwise dispose of the common stock described in this prospectus in a number of different ways and at varying prices. See "Plan of Distribution" for more information about how the selling stockholder may sell or otherwise dispose of the common stock being registered pursuant to this prospectus. The selling stockholder is an "underwriter" within the meaning of Section 2(a)(11) of the Securities Act of 1933, as amended (the "Securities Act").

We will pay the expenses incurred in registering under the Securities Act the offer and sale of the common stock to which this prospectus relates by the selling stockholder, including legal and accounting fees. See "Plan of Distribution".

Our common stock is currently listed on the Nasdaq Capital Market ("Nasdaq") under the symbol "PSTV." On November 8, 2023, the closing price of our common stock, as reported on Nasdaq, was \$1.59 per share.

Investing in our securities involves a high degree of risk. These risks are described in the "Risk Factors" section on page 12 of this prospectus. You should also consider the risk factors described or referred to in any documents incorporated by reference in this prospectus, and in any applicable prospectus supplement, before investing in these securities.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is _____, 2023

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ABOUT THIS PROSPECTUS

This prospectus forms part of a registration statement that we filed with the Securities and Exchange Commission (the “SEC”), and that includes exhibits that provide more detail of the matters discussed in this prospectus. You should read this prospectus and the related exhibits filed with the SEC, together with the additional information described under the headings “Where You Can Find More Information” and “Incorporation by Reference” before making your investment decision.

You should rely only on the information provided in this prospectus or in a prospectus supplement or any free writing prospectuses or amendments thereto. Neither we, nor the selling stockholder, have authorized anyone else to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. You should assume that the information in this prospectus is accurate only as of the date hereof. Our business, financial condition, results of operations and prospects may have changed since that date.

Neither we, nor the selling stockholder, are offering to sell or seeking offers to purchase these securities in any jurisdiction where the offer or sale is not permitted. We have not done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the securities as to distribution of the prospectus outside of the United States.

Unless the context otherwise requires, references in this prospectus to “Plus,” “the Company,” “we,” “us” and “our” refer to Plus Therapeutics, Inc. Our logo and all product names are our common law trademarks. Solely for convenience, trademarks and tradenames referred to in this prospectus may appear without the ® or ™ symbols, but such references are not intended to indicate in any way that we will not assert, to the fullest extent under applicable law, our rights, or that the applicable owner will not assert its rights, to these trademarks and tradenames.

PROSPECTUS SUMMARY

This summary contains basic information about us and this offering. Because it is a summary, it does not contain all of the information that you should consider before investing. Before you decide to invest in our common stock, you should read this entire prospectus carefully, including the section entitled “Risk Factors,” and any documents incorporated by reference.

Our Business

Overview

We are a U.S. pharmaceutical company developing targeted radiotherapeutics with advanced platform technologies for central nervous system (“CNS”) cancers. Our novel radioactive drug formulations and therapeutic candidates are designed to deliver safe and effective doses of radiation to tumors. To achieve this, we have developed innovative approaches to drug formulation, including encapsulating radionuclides such as rhenium isotopes with nanoliposomes and microspheres. Our formulations are intended to achieve elevated patient absorbed radiation doses and extend retention times such that the clearance of the isotope occurs after significant and essentially complete radiation decay, which will contribute and provide less normal tissue/organ exposure and improved safety margins.

Traditional approaches to radiation therapy for cancer such as external beam radiation have many disadvantages including continuous treatment for four-to-six weeks (which is onerous for patients), that the radiation damages healthy cells and tissue, and that the amount of radiation delivered is very limited and, therefore, is frequently inadequate to fully destroy the cancer.

Our targeted radiotherapeutic platform and unique investigational drugs have the potential to overcome these disadvantages by directing higher, more powerful radiation doses at the tumor—and only the tumor—potentially in a single treatment. By minimizing radiation exposure to healthy tissues while simultaneously maximizing locoregional delivery and, thereby, efficacy, we hope to reduce the radiation toxicity for patients, improving their quality of life and life expectancy. Our radiotherapeutic platform, combined with advances in surgery, nuclear medicine, interventional radiology, and radiation oncology, affords us the opportunity to target a broad variety of cancer types.

Our lead radiotherapeutic candidate, rhenium (^{186}Re) obisbameda (formerly “ ^{186}RNL ”), is designed specifically for CNS cancers including recurrent glioblastoma (“GBM”), leptomeningeal metastases (“LM”), and pediatric brain cancers (“PBC”) by direct localized delivery utilizing approved standard-of-care tissue access such as with convection-enhanced delivery (“CED”) and intraventricular brain (Ommaya reservoir) catheters. Our acquired radiotherapeutic candidate, Rhenium-188 NanoLiposome Biodegradable Alginate Microsphere (“ $^{188}\text{RNL-BAM}$ ”) is designed to treat many solid organ cancers including primary and secondary liver cancers by intra-arterial injection.

Our headquarters and manufacturing facilities are in Texas and are in proximity to world-class cancer institutions and researchers. Our dedicated team of engineers, physicians, scientists, and other professionals are committed to advancing our targeted radiotherapeutic technology for the benefit of cancer patients and healthcare providers worldwide and our current pipeline is focused on treating rare and difficult-to-treat cancers with significant unmet medical needs.

In addition to our headquarters in Austin, we have an established, GMP-validated research and development and manufacturing facility in San Antonio, Texas, tailored to produce Current Good Manufacturing Practice (“cGMP”) rhenium (^{186}Re) obisbameda. We have built a robust supply chain through strategic partnerships that enable the development, manufacturing and future potential commercialization of our products. Our current

supply chain and key partners are positioned to supply cGMP rhenium (186Re) obisbameda for ongoing and planned Phase 2 and Phase 3 clinical trials in patients with GBM, LM and PBC.

Pipeline

Our most advanced investigational drug, rhenium (186Re) obisbameda, is a patented radiotherapy potentially useful for patients with CNS and other cancers. Preclinical study data describing the use of rhenium (186Re) obisbameda for several cancer targets have been published in peer-reviewed journals and reported at a variety of medical society peer-reviewed meetings. Besides, GBM, LM and PBC, rhenium (186Re) obisbameda has been reported to have potential applications for head and neck cancer, ovarian cancer, breast cancer and peritoneal metastases.

The rhenium (186Re) obisbameda technology was part of a licensed radiotherapeutic portfolio that we acquired from NanoTx, Corp. on May 7, 2020. The licensed radiotherapeutic has been evaluated in preclinical studies for several cancer targets and we have an active \$3.0 million award from U.S. National Institutes of Health/National Cancer Institute which is expected to provide financial support for the continued clinical development of rhenium (186Re) obisbameda for recurrent GBM through the completion of a Phase 2 clinical trial including enrollment of up to 55 patients.

On August 29, 2022, we announced feedback from a Type C meeting with the U.S. Food and Drug Administration (the “FDA”) regarding Chemistry, Manufacturing and Controls (“CMC”) practices. The meeting focused on our cGMP clinical and commercial manufacturing process for our lead investigational targeted radiotherapeutic, BMEDA-chelated rhenium (186Re) obisbameda, for recurrent GBM.

The FDA indicated agreement with our proposed application of cGMP guidance for radiotherapeutics, small molecule drug products and liposome drug products for our novel rhenium (186Re) obisbameda in support of ongoing and future GBM clinical trials, manufacturing scale up, and commercialization. Alignment with the FDA includes support of our proposed controls and release strategy for new drug substance and new drug product. Because this product is identical for recurrent GBM, LM, and PBC, we believe alignment will be consistent for rhenium (186Re) obisbameda used in other clinical development programs, including LM and PBC.

Rhenium (186Re) obisbameda versus External Beam Radiation Therapy for Recurrent GBM

Rhenium (186Re) obisbameda is a novel injectable radiotherapy designed to deliver targeted, high dose radiation directly into GBM tumors in a safe, effective, and convenient manner that may ultimately prolong patient survival. Rhenium (186Re) obisbameda is composed of the radionuclide Rhenium-186 and a nanoliposomal carrier, and is infused in a highly targeted, controlled fashion, directly into the tumor via precision brain mapping and CED catheters. Potential benefits of rhenium (186Re) obisbameda compared to standard external beam radiotherapy include:

- The rhenium (186Re) obisbameda radiation dose delivered to patients may be up to 20 times greater than what is possible with commonly used external beam radiation therapy (“EBRT”), which, unlike EBRT and proton beam devices, spares normal tissue and the brain from radiation exposure.
- Rhenium (186Re) obisbameda can be visualized in real-time during administration, possibly giving clinicians better control of radiation dosing, distribution and retention.
- Rhenium (186Re) obisbameda potentially more effectively treats a bulk tumor and microscopic disease that has already invaded healthy tissue.
- Rhenium (186Re) obisbameda is infused directly into the targeted tumor by CED catheter insertion using MRI guided software to avoid critical patient neurological structures and neural pathways and

also bypasses the blood brain barrier, which delivers the therapeutic product where it is needed. Importantly, it reduces radiation exposure to healthy cells, in contrast to EBRT which passes through normal tissue to reach the tumor, continuing its path through the tumor, hence being less targeted and selective.

- Rhenium (¹⁸⁶Re) obisbameda is given during a single, short, in-patient hospital visit, and is available in all hospitals with nuclear medicine and neurosurgery, while EBRT requires out-patient visits five days a week for approximately four-to-six weeks.

ReSPECT-GBM Trial for Recurrent GBM

Recurrent GBM is the most common, complex, and aggressive primary brain cancer in adults. In the U.S., there are more than 13,000 GBM cases diagnosed and approximately 10,000 patients succumb to the disease each year. The average length of overall survival (“OS”) for GBM patients is eight months, with a one-year survival rate of 40.8% and a five-year survival rate of only 6.8% and these estimates vary and are lower in some publications. GBM routinely presents with headaches, seizures, vision changes and other significant neurological complications, with a significant compromise in quality of life. Despite the best available medical treatments, the disease remains incurable. Even after efforts to manage the presenting signs and symptoms and completely resect the initial brain tumor, some microscopic disease almost always remains and tumor regrowth occurs within months. Approximately 90% or more of patients with primary GBM experience tumor recurrence. Complete surgical removal of GBM is usually not possible and GBM is often resistant or quickly develops resistance to most available current and investigational therapies. Even today, the treatment of GBM remains a significant challenge and it has been nearly a decade since the FDA approved a new therapy for this disease, and these more recent approvals have not improved GBM patients’ OS over past decades, and significant unmet medical need persists.

For recurrent GBM, there are few currently approved treatments, which in the aggregate, provide only marginal survival benefit. Furthermore, these therapies are associated with significant side effects, which limit dosing and prolonged use.

While EBRT has been shown to be safe and has temporary efficacy in many malignancies, including GBM, typically at absorbed, fractionated radiation dose of ~30 Gray in GBM, this maximum possible administered dose is always limited by toxicity to the normal tissues surrounding the malignancy, and because EBRT requires fractionation to manage toxicity and maximum EBRT limits are typically reached before long-term efficacy reached. Because of this limitation, EBRT cannot provide a cure or long term control of GBM and GBM always recurs within months after EBRT. In contrast, locally delivered and targeted radiopharmaceuticals that precisely deliver radiation in the form of beta particles such as Iodine-131 for thyroid cancer, are known to be safe and effective and minimize exposure to normal cells and tissues especially with optimal administered dose and minimizing exposure to normal tissue. The locally delivered rhenium (¹⁸⁶Re) obisbameda is designed for and provides patient tolerability and safety. Though no rhenium (¹⁸⁶Re) obisbameda head-to-head trial with chemo, immune, EBRT or systemic radiopharmaceutical products have been conducted, patient tolerability and safety considerations have been reported as expected.

Interim results from our ongoing Phase 1/2a ReSPECT-GBM trial (ClinicalTrials.gov NCT01906385) show that the beta particle energy from our lead investigational drug rhenium (¹⁸⁶Re) obisbameda has provided preliminary positive data and utility in treating GBM and potential other malignancies. More specifically, the preliminary data from our Phase 1/2a ReSPECT-GBM trial suggests that radiation, in the form of high energy beta particles or electrons, can be effective against GBM. Thus far, we have been able to deliver up to 740 Gy of absorbed radiation to tumor tissue in humans, without significant or dose limiting toxicities and with what we believe has the capability to go higher if required. In comparison, current EBRT protocols for recurrent GBM typically recommend a total maximum radiation dose of about ~30-35 Gray.

In September 2020, the FDA granted both Orphan Drug designation and Fast Track designations to rhenium (186Re) obisbameda for the treatment of patients with GBM. In November 2021, the FDA granted Fast Track designation for rhenium (186Re) obisbameda for the treatment of LM.

Rhenium (186Re) obisbameda is under clinical investigation in a multicenter, sequential cohort, open-label, volume and dose escalation study of the safety, tolerability, and distribution of rhenium (186Re) obisbameda given by CED catheters to patients with recurrent or progressive malignant glioma after standard surgical, radiation, and/or chemotherapy treatment (NCT01906385). The study uses a standard, modified 3x3 Fibonacci dose escalation, followed by a planned Phase 2 expansion trial at the maximum tolerated dose (“MTD”)/maximum feasible dose (“MFD”) or non-dose limiting toxicity (“DLT”) if MTD is not reached, to determine efficacy. The trial is funded through Phase 2 in large part by a NIH/NCI grant. These investigations have not reached DLT or MTD/MFD and the study is in its eighth dosing administration cohort. Due to the observation of a preliminary efficacy signal, we have initiated in parallel a Phase 2, non-DLT dose trial pursuant to the currently funded NIH/NCI grant. This trial will begin at the current non-DLT rhenium (186Re) obisbameda dose and will expand exploring higher radiation doses in larger volumes to treat larger tumors. Additionally, two or more rhenium (186Re) obisbameda administrations, if indicated, will be evaluated, and reviewed with the FDA, as well as expanded safety, imaging and efficacy data to support a planned future registrational trial.

On September 6, 2022, we announced a summary of our Type C clinical meeting with the FDA that focused on the ReSPECT-GBM trial. The FDA agreed with us that the ReSPECT-GBM clinical trial should proceed to the planned Phase 2. The key focus areas of clinical investigation of the Phase 2 trial will be (1) further dose exploration, including both increased dosing and multiple doses, and (2) collecting additional safety and efficacy data to inform the design of a future registrational trial. Because no DLT administered doses were observed, the FDA and we also agreed to continue to dose cohort eight. There was further agreement with the FDA that in a planned future registrational trial, overall survival should be used as the primary endpoint. We agreed with the FDA to hold future meeting(s) to consider the use of external data to augment the use of a control arm in the registrational trial.

On January 18, 2023, we announced that the first patient has been dosed in the ReSPECT-GBM Phase 2b dose expansion clinical trial evaluating rhenium obisbameda for the treatment of recurrent GBM. The Phase 2b trial is expected to enroll up to 31 total patients with small- to medium-sized tumors in approximately 24 months.

In June 2023, we presented data regarding the safety and feasibility results from our Phase 1/2 Clinical Trial of 186RNL (Rhenium-186 Nanoliposome) (186) Obisbameda in Recurrent Glioma: The ReSPECT-GBM Trial at the Society of Nuclear Medicine & Molecular Imaging Annual Meeting.

On March 31, 2022, we entered into a Sales Order (the “Sales Order”) with Medidata Solutions, Inc. (“Medidata”), pursuant to which Medidata built a Synthetic Control Arm[®] (“SCA”) platform that facilitates the use of historical clinical data to incorporate into our Phase 2 clinical trial of rhenium (186Re) obisbameda in GBM. The Sales Order had a term of six months. Work under this Sales Order has been completed. As part of this collaboration, we jointly submitted with Medidata a historical clinical trials control arm methodology abstract (“HCA”) to the American Society of Clinical Oncology (“ASCO”) which was accepted for publication, further strengthening this collaboration and allowing applications to advance GBM development. We plan to use the HCA for breakthrough therapy designation and Phase 2 and/or a pivotal or registrational Phase 3 trial.

ReSPECT-LM Clinical Trial for LM

LM is a rare complication of cancer in which the disease spreads to the membranes (meninges) surrounding the brain and spinal cord. The incidence of LM is growing and occurs in approximately 5% or more of people with late-stage cancer, or 110,000 people in the U.S. each year. It is highly lethal with an average one-year survival of just 7%. All solid cancers, particularly breast, lung, GI, and melanoma, have the potential to spread to the leptomeninges.

The ReSPECT-LM Phase 1 clinical trial (ClinicalTrials.gov NCT05034497) was preceded with preclinical studies in which tolerance to doses of rhenium (186Re) obisbameda as high as 1,075 Gy were shown in animal models with LM without significant observed toxicity. Furthermore, treatment led to a marked reduction in tumor burden in both C6 and MDA-231 LM models.

Upon receiving acceptance of our Investigational New Drug application and Fast Track designation by the FDA for rhenium (186Re) obisbameda for the treatment of LM, we initiated the trial and began screening patients for the ReSPECT-LM Phase 1 clinical trial in Q4 2021. The ReSPECT-LM is a multi-center, sequential cohort, open-label, dose escalation study evaluating the safety, tolerability, and efficacy of a single-dose application of rhenium (186Re) obisbameda administered through intrathecal infusion to the ventricle of patients with LM after standard surgical, radiation, and/or chemotherapy treatment. The primary endpoint of the study is the incidence and severity of adverse events and dose limiting toxicities.

On September 19, 2022, we entered into a Cancer Research Grant Contract (the “CPRIT Contract”), effective as of August 31, 2022, with CPRIT, pursuant to which CPRIT will provide us a grant of up to \$17.6 million (the “CPRIT Grant”) over a three-year period to fund the continued development of rhenium (186Re) obisbameda for the treatment of patients with LM through Phase 2 of the ReSPECT LM clinical trial. The CPRIT Grant is subject to customary CPRIT funding conditions, including, but not limited to, a matching fund requirement (one dollar from us for every two dollars awarded by CPRIT), revenue sharing obligations upon commercialization of rhenium (186Re) obisbameda based on specific dollar thresholds until CPRIT receives the aggregate amount of 400% of the proceeds awarded under the CPRIT Grant, and certain reporting requirements.

Interim results showed that a single treatment with rhenium (186Re) obisbameda showed a consistent decreased CSF tumor cell count/ml and was very well tolerated by all LM patients. Rhenium (186Re) obisbameda is an outpatient administration and treatment and is easily and safely administered through a standard intraventricular catheter (Ommaya Reservoir), distributed promptly throughout the CSF, and with durable retention in the leptomeninges at least through day seven. All patients have shown well tolerated prompt and durable rhenium (186Re) obisbameda distribution throughout the subarachnoid space. Cohort 3 is currently enrolling, with protocol defined FDA review to allow proceeding with Cohort 4-7 expansion after the protocol defined observation period and independent DSMB review.

A single dose of rhenium (186Re) obisbameda at 6.6 millicurie (“mCi”) in 5.0 mL, in Cohort 1, achieved absorbed doses of 18.7 to 29.0 Gy to the ventricles and cranial subarachnoid spaces, respectively. Cohort 2 has also completed with a 13.2 mCi administered dose in 5ml and was also well tolerated. Cohort 3 enrolled three patients through early April 2023 with a 26.4 mCi administered dose.

On August 10, 2023, we presented data from the ReSPECT-LM clinical trial of rhenium (186Re) obisbameda at the Society for Neuro Oncology ASCO CNS Cancer Conference.

ReSPECT-PBC Clinical Trial for Pediatric Brain Cancer

The average annual age adjusted mortality rate for children aged 0-14 for malignant brain (and other CNS) tumors is 0.71/100,000, making it the most common cause of death and cancer death in this age group. The 2021 World Health Organization Classification of CNS Tumors classifies gliomas, glioneuronal tumors, and neuronal tumors into six different families: (1) adult-type diffuse gliomas; (2) pediatric-type diffuse low-grade gliomas; (3) pediatric-type diffuse high-grade gliomas (“HGG”); (4) circumscribed astrocytic gliomas; (5) glioneuronal and neuronal tumors; and (6) ependymomas.

In August 2021, we announced plans for treating pediatric brain cancer at the 2021 American Association of Neurological Surgeons Annual Scientific Meeting. In July 2021, we reported that we had received FDA feedback pertaining to a pre-IND meeting briefing package in which the FDA stated that we are not required to perform any additional preclinical or toxicology studies.

Since the initial FDA feedback and receiving important adult GBM data and experience with rhenium (^{186}Re) obisbameda and follow-up communications with the FDA, we plan to submit a pediatric brain tumor IND to investigate the use of rhenium (^{186}Re) obisbameda in two pediatric brain cancers, high-grade glioma and ependymoma, in the second or third quarter of 2023.

Pediatric high-grade gliomas can be found almost anywhere within the CNS; however, they are most commonly found within the supratentorium. The highest incidence of supratentorial, high-grade gliomas in pediatrics appears to occur in children aged 15 to 19 years, with a median age of approximately nine years. Overall, pediatric high-grade glioma confers a three-year progression free survival (“PFS”) of $11 \pm 3\%$ and three-year OS of $22\% \pm 5\%$. One-year PFS is as low as 40% in recent trials. Ependymomas are slow-growing central nervous system tumors that involve the ventricular system. Diagnosis is based on MRI and biopsy and survival rate depends on tumor grade and how much of the tumor can be removed. Grade II pathology was associated with significantly improved OS compared to Grade III (anaplastic) pathology (five-year OS = $71 \pm 5\%$ vs. $57 \pm 10\%$; $p = 0.026$). Gross total resection compared to subtotal resection was associated with significantly improved OS (five-year OS = $75 \pm 5\%$ vs. $54 \pm 8\%$; $p = 0.002$).

Overall, pediatric HGG and ependymoma are extremely difficult-to-treat pediatric brain tumors, frequently aggressive, and in recurrent settings, carry an extremely poor prognosis.

Rhenium-188 NanoLiposome Biodegradable Alginate Microsphere Technology

In January 2022, we announced that we licensed Biodegradable Alginate Microsphere (“BAM”) patents and technology from The University of Texas Health Science Center at San Antonio (“UTHSA”) to expand our tumor targeting capabilities and precision radiotherapeutics pipeline. We intend to combine our Rhenium NanoLiposome technology with the BAM technology to create a novel radioembolization technology. Initially, we intend to utilize the Rhenium-188 isotope, ^{188}RnL -BAM for the intra-arterial embolization and local delivery of a high dose of targeted radiation for a variety of solid organ cancers such as hepatocellular cancer, hepatic metastases, pancreatic cancer and many others.

Preclinical data from an *ex vivo* embolization experiment in which Technetium $^{99\text{m}}$ -BAM was intra-arterially delivered to a bovine kidney perfusion model was presented at the recent 2021 Society of Interventional Radiology Annual Scientific Meeting. The study concluded that the technology required for radiolabeling BAM could successfully deliver, embolize and retain radiation in the target organ. ^{188}RnL -BAM is a preclinical investigational drug we intend to further develop and move into clinical trials. Specifically, in 2022, we transferred the ^{188}RnL -BAM technology from UTHSA, and began planning to develop the drug product, and complete early preclinical studies to support a future FDA IND submission. Our intended initial clinical target is liver cancer which is the sixth most common and third deadliest cancer worldwide. It is a rare disease with increasing U.S. annual incidence (42,000) and deaths (30,000).

Grant Agreement with CPRIT

As noted above in the LM development discussion, on September 19, 2022, we entered into a Cancer Research Grant Contract (the “CPRIT Contract”), effective as of August 31, 2022, with CPRIT, pursuant to which CPRIT will provide us a grant of up to \$17.6 million (the “CPRIT Grant”) over a three-year period to fund the continued development of rhenium (^{186}Re) obisbameda for the treatment of patients with LM. The CPRIT

Grant is subject to customary CPRIT funding conditions, including, but not limited to, a matching fund requirement (one dollar from Plus Therapeutics for every two dollars awarded by CPRIT), revenue sharing obligations upon commercialization of rhenium (186Re) obisbameda based on specific dollar thresholds until CPRIT receives the aggregate amount of 400% of the proceeds awarded under the CPRIT Grant, and certain reporting requirements.

Recent Financings

ATM Program

On September 9, 2022, we entered into an Equity Distribution Agreement (the “September 2022 Distribution Agreement”) with Canaccord Genuity LLC (“Canaccord”), pursuant to which we may issue and sell, from time to time, shares of our common stock having an aggregate offering price of up to \$5,000,000, depending on market demand, with Canaccord acting as an agent for sales. Sales of our common stock may be made by any method permitted by law deemed to be an “at the market offering” as defined in Rule 415(a)(4) of the Securities Act of 1933, as amended (the “Securities Act”), including, without limitation, sales made directly on or through the Nasdaq Capital Market. Canaccord will use its commercially reasonable efforts to sell common stock requested by the Company to be sold on its behalf, consistent with Canaccord’s normal trading and sales practices, under the terms and subject to the conditions set forth in the September 2022 Distribution Agreement. We have no obligation to sell any of our common stock. We may instruct Canaccord not to sell any common stock if the sales cannot be effected at or above the price designated by us from time to time and we may at any time suspend sales pursuant to the September 2022 Distribution Agreement. From January 1, 2023 through September 30, 2023, the Company issued 1,819,993 shares under the September 2022 Distribution Agreement for net proceeds of approximately \$4.3 million. The Company has reached the capacity for sales of shares under the September 2022 Distribution Agreement.

The Purchase Agreement with Lincoln Park

On August 2, 2022, we entered into the Purchase Agreement with Lincoln Park, pursuant to which Lincoln Park has agreed to purchase from us up to an aggregate of \$50.0 million of our common stock (subject to certain limitations) from time to time over the term of the Purchase Agreement. Also on August 2, 2022, we entered into a registration rights agreement with Lincoln Park, which we refer to in this prospectus as the Registration Rights Agreement, pursuant to which we filed with the SEC the registration statement that includes this prospectus to register for resale under the Securities Act of 1933, as amended, or the Securities Act, the shares of our common stock that have been and may be issued to Lincoln Park under the Purchase Agreement.

This prospectus covers the resale of up to 1,300,000 shares of our common stock that we have reserved for issuance and sale to Lincoln Park under the Purchase Agreement from time to time. Under the 2022 Registration Statement, we registered 633,333 shares of our common stock comprised of: (i) 32,846 shares of our common stock that we initially issued to Lincoln Park as Initial Commitment Shares for making its irrevocable commitment to purchase shares of our common stock under the Purchase Agreement at our direction, and (ii) up to 600,486 that we had reserved for issuance and sale to Lincoln Park under the Purchase Agreement from time to time from thereafter at our determination. Under the August 2023 Registration Statement, we registered 1,500,000 shares of our common stock that we may issue and sell from time to time, at our sole discretion, to Lincoln Park under the Purchase Agreement. As of November 8, 2023, we have issued and sold an aggregate of 677,167 shares of common stock pursuant to the Purchase Agreement and under the Prior Registration Statements.

As consideration for Lincoln Park’s irrevocable commitment to purchase shares of our common stock upon the terms of and subject to satisfaction of the conditions set forth in the Purchase Agreement, we paid \$125,000 in cash as an Initial Commitment Fee and issued 32,846 Commitment Shares to Lincoln Park in consideration for

its commitment to purchase shares of our common stock at our direction under the Purchase Agreement. We have also agreed to pay an Additional Commitment Fee of \$625,000, which we may elect to pay in cash or shares of our common stock or any combination thereof, upon our receipt of \$25.0 million aggregate gross proceeds from sales of common stock to Lincoln Park under the Purchase Agreement. Through November 8, 2023, \$4.2 million of common stock have been sold under the Prior Registration Statements.

We did not have the right to commence sales of our common stock to Lincoln Park under the Purchase Agreement until the Commencement Date (as defined in the Purchase Agreement). From and after the Commencement Date, we may, from time to time and at our sole discretion for a period of 36 months after the Commencement Date, on any business day that we select on which the closing sale price of our common stock equals or exceeds \$1.00 per share, direct Lincoln Park to purchase up to 6,666 shares of our common stock, (or, if higher, such number of shares of our common stock such that the limit equals (or as closely equals without exceeding) \$150,000), which amount may be increased depending on the market price of our common stock at the time of sale, subject to a maximum commitment of \$1,000,000 per purchase, which we refer to in this prospectus as “Regular Purchases.” The maximum number of shares we may sell to Lincoln Park in a Regular Purchase may be increased to up to 20,000 shares, provided that the closing sale price of our common stock on the applicable purchase date is not below certain threshold prices set forth in the Purchase Agreement. In addition, Lincoln Park has committed to purchase other “accelerated amounts” and/or “additional accelerated amounts” under certain circumstances. We control the timing and amount of any sales of our common stock to Lincoln Park. The purchase price of the shares of our common stock that may be sold to Lincoln Park in Regular Purchases under the Purchase Agreement is based on the market price of our common stock at or preceding the time of sale as computed under the Purchase Agreement. The purchase price per share is equitably adjusted as provided in the Purchase Agreement for any reorganization, recapitalization, non-cash dividend, stock split, or other similar transaction as set forth in the Purchase Agreement. We may at any time in our sole discretion terminate the Purchase Agreement without fee, penalty or cost upon one business day notice. There are no restrictions on future financings, rights of first refusal, participation rights, penalties or liquidated damages in the Purchase Agreement or Registration Rights Agreement, other than a prohibition on our entering into certain types of transactions that are defined in the Purchase Agreement as “Variable Rate Transactions.” Lincoln Park may not assign or transfer its rights and obligations under the Purchase Agreement.

As of September 30, 2023, there were 4,522,656 shares of our common stock outstanding, of which 4,475,782 shares of our common stock were held by non-affiliates, and which number includes shares previously issued to Lincoln Park, including the Commitment Shares. If all of the 1,300,000 shares offered by Lincoln Park under this prospectus were issued and outstanding, such shares would represent approximately 22.3% of the total number of shares of our common stock outstanding and approximately 22.5% of the total number of outstanding shares held by non-affiliates, in each case as of September 30, 2023. The Purchase Agreement provides that we may sell up to an aggregate of \$50.0 million of our common stock to Lincoln Park, of which we have previously issued \$4.2 million. We have filed the registration statement that includes this prospectus so that we may issue and sell to Lincoln Park up to 1,300,000 shares of our common stock from time to time from and after the date of this prospectus through sales under the Purchase Agreement. Depending on the market prices of our common stock at the time we elect to issue such shares to Lincoln Park under the Purchase Agreement, we may need to sell more shares to Lincoln Park than are offered under this prospectus and the Prior Registration Statements to receive aggregate gross proceeds equal to the \$50.0 million total commitment of Lincoln Park under the Purchase Agreement, in which case we must again register for resale under the Securities Act additional shares of our common stock, which could cause additional substantial dilution to our stockholders. If in satisfaction of the Additional Commitment Fee, we issue additional shares of our common stock to Lincoln Park, or Additional Commitment Shares, we would also need to register those shares for resale under the Securities Act pursuant to a separate resale registration statement, which would also cause additional dilution to our shareholders. The number of shares ultimately offered for resale by Lincoln Park is dependent upon the number of shares we issue and sell to Lincoln Park under the Purchase Agreement.

Prior to entering into the Purchase Agreement with Lincoln Park, we received stockholder approval at our 2022 Annual Meeting of Stockholders that was held on May 16, 2022 (the “Annual Meeting”) pursuant to Nasdaq Listing Rules 5635(a), 5635(b) and 5635(d) to permit issuances of our common stock (including the issuance of more than 19.99% of our common stock) to Lincoln Park pursuant to the Purchase Agreement. Based on the closing price of our common stock of \$1.00 per share on March 22, 2022 (the lowest closing sale price between January 1, 2022 and the date of the proxy statement filed in connection with the Annual Meeting, as reported on Nasdaq.com), the maximum number of shares we could issue and sell under the Purchase Agreement is approximately 3,830,000 shares. Accordingly, we requested and received stockholder approval for the issuance of up to 3,830,000 shares of our common stock in the aggregate under the Purchase Agreement. We would seek additional stockholder approval before issuing more than an aggregate of 3.83 million shares under the Purchase Agreement.

The Purchase Agreement also prohibits us from directing Lincoln Park to purchase any shares of common stock if those shares, when aggregated with all other shares of our common stock then beneficially owned by Lincoln Park and its affiliates, would result in Lincoln Park and its affiliates having beneficial ownership, at any single point in time, of more than 4.99% of the then total outstanding shares of our common stock, as calculated pursuant to Section 13(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and Rule 13d-3 thereunder, which limitation we refer to as the Beneficial Ownership Cap.

There are substantial risks to our stockholders as a result of the sale and issuance of common stock to Lincoln Park under the Purchase Agreement. These risks include substantial dilution, significant declines in our stock price and our inability to draw sufficient funds when needed. See “Risk Factors.” The sale of our common stock to Lincoln Park under the Purchase Agreement will not affect the rights or privileges of our other stockholders, except that the economic and voting interests of our existing stockholders will be diluted as a result of any such sale. Although the number of shares of common stock that our other stockholders own will not decrease, the shares owned by our other stockholders will represent a smaller percentage of our total outstanding shares after any such sale to Lincoln Park under the Purchase Agreement.

Corporate Information

We were initially formed as a California general partnership in July 1996 and incorporated in the State of Delaware in May 1997. We were formerly known as Cytori Therapeutics, Inc., before that as MacroPore Biosurgery, Inc. and before that as MacroPore, Inc. On July 20, 2019 we changed our name from Cytori Therapeutics, Inc. to Plus Therapeutics, Inc. Our corporate offices are located at 4200 Marathon Blvd., Suite 200, Austin, Texas 78756. Our telephone number is (737) 255-7194. We maintain a website at www.plustherapeutics.com. The contents of our website are not part of this prospectus and the references in this prospectus and the documents we have incorporated by reference to our website do not constitute incorporation by reference into this prospectus of the information contained therein.

THE OFFERING

Shares of our common stock offered by the selling stockholder	Up to 1,300,000 shares of our common stock, which we may issue and sell to Lincoln Park from time to time, at our sole discretion, during the 36-month period that began on the Commencement Date in accordance with the Purchase Agreement.
Shares of our common stock outstanding prior to this offering (as of September 30, 2023)	4,522,656 shares of our common stock.
Shares of our common stock to be outstanding after this offering	5,822,656 shares of our common stock, assuming the sale of all the shares of common stock registered hereunder to Lincoln Park under the Purchase Agreement. The actual number of shares outstanding after this offering will vary depending upon the actual number of shares we sell to Lincoln Park under the Purchase Agreement after the date of this prospectus.
Use of proceeds	We will receive no proceeds from the sale of shares of our common stock by Lincoln Park in this offering. We may receive up to \$50.0 million aggregate gross proceeds under the Purchase Agreement from any sales of shares of our common stock we make to Lincoln Park pursuant to the Purchase Agreement, assuming that we sell the full amount of our common stock that we have the right, but not the obligation to sell to Lincoln Park under the Purchase Agreement. Through November 8, 2023, we have received \$4.2 million under the Purchase Agreement. Any proceeds that we receive from sales of shares of our common stock to Lincoln Park under the Purchase Agreement will be used for working capital and general corporate purposes. See “Use of Proceeds.”
Nasdaq symbol for our common stock	“PSTV”
Risk factors	This investment involves a high degree of risk. See “Risk Factors” beginning on page 11 of this prospectus for a discussion of factors you should carefully consider before deciding to invest in our securities.

Unless otherwise noted, the number of shares of common stock to be outstanding immediately after this offering is based on 4,522,656 shares outstanding as of September 30, 2023 and excludes, as of September 30, 2023:

- 78,334 shares of common stock issuable upon exercise of stock options outstanding under our equity incentive plans, with a weighted-average exercise price of \$68.10 per share;
- 6,023 shares of common stock reserved for future issuance under our 2015 New Employee Incentive Plan;
- 179,640 shares of common stock reserved for future issuance under our 2020 Stock Incentive Plan;

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- 398 and 27,792 shares of common stock issuable upon conversion of 1,014 shares of Series B Convertible Preferred Stock and 938 shares of Series C Preferred Stock, respectively;
- 142,733 shares of common stock issuable upon the exercise of warrants to purchase common stock, with a weighted-average exercise price of \$34.10 per share; and
- up to 1,423,319 shares of our common stock available to be sold as of November 8, 2023, pursuant to the Purchase Agreement under the August 2023 Registration Statement.

RISK FACTORS

Investing in our securities involves a high degree of risk. Before making an investment decision with respect to our securities, we urge you to carefully consider the risks described below and in the “Risk Factors” sections of our most recent Annual Report on Form 10-K and Quarterly Reports on Form 10-Q, as well as our Current Reports on Form 8-K, filed with the SEC and incorporated by reference in this prospectus, and the other information contained in this prospectus. The risks and uncertainties incorporated by reference into this prospectus or described below are not the only ones we face. Additional risks and uncertainties not presently known or which we consider immaterial as of the date hereof may also materially harm our business and could result in a complete loss of your investment. If any of the matters discussed in the following risk factors were to occur, our business, financial condition, results of operations, cash flows, or prospects could be materially and adversely affected, the market price of our common stock could decline, and you could lose all or part of your investment in our securities.

Risks Related to the Offering

The sale or issuance of our common stock to Lincoln Park may cause dilution to our other stockholders and the sale of the shares of common stock acquired by Lincoln Park, or the perception that such sales may occur, could cause the price of our common stock to fall.

Lincoln Park has committed to purchase up to \$50.0 million of our common stock under the Purchase Agreement, of which they have previously purchased \$4.2 million through November 8, 2023. The purchase price for the shares that we may sell to Lincoln Park under the Purchase Agreement remains subject to the pricing formula in the Purchase Agreement and will fluctuate based on the price of our common stock. Depending on market liquidity at the time, any future sales of such shares may cause the trading price of our common stock to fall.

We generally have the right to control the timing and amount of any sales of our shares to Lincoln Park. Additional sales of our common stock, if any, to Lincoln Park will depend upon market conditions, the trading price of our common stock, determinations by us as to the appropriate sources of funding for our company and its operations and other factors to be determined by us. We may ultimately decide to sell to Lincoln Park all, some, or none of the additional shares of our common stock that may be available for us to sell pursuant to the Purchase Agreement. If and when we do sell additional shares to Lincoln Park or issue Additional Commitment Shares to Lincoln Park, after Lincoln Park has acquired the shares, Lincoln Park may resell all, some or none of those shares at any time or from time to time in its discretion. Therefore, additional sales and issuances to Lincoln Park by us could result in substantial dilution to the interests of other holders of our common stock. Additionally, the sale or issuances of a substantial number of shares of our common stock to Lincoln Park, or the anticipation of such sales, could make it more difficult for us to sell equity or equity-related securities in the future at a time and at a price that we might otherwise wish to effect sales.

We may not have access to the full amount available under the Purchase Agreement with Lincoln Park. We may require additional financing to sustain our operations, without which we may not be able to continue operations, and the terms of subsequent financings may adversely impact our stockholders.

We may direct Lincoln Park to purchase up to \$50.0 million worth of shares of our common stock from time to time under the Purchase Agreement over a 36-month period generally in amounts up to 6,666 shares of our common stock (or, if higher, such number of shares of our common stock such that the limit equals (or as closely equals without exceeding) \$150,000), which may be increased to up to 20,000 shares of our common stock depending on the market price of our common stock at the time of sale, provided that Lincoln Park’s committed obligation under such single Regular Purchase shall not exceed \$1,000,000. If and when we receive \$25.0 million aggregate gross proceeds from sales of common stock to Lincoln Park under the Purchase Agreement, we are also required to pay the Additional Commitment Fee, which we may elect to pay in cash or Additional

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Commitment Shares, provided that we can only issue Additional Commitment Shares if we have registered those shares for resale under the Securities Act pursuant to a separate resale registration statement.

Depending on the prevailing market price of our common stock, we may not be able to sell shares to Lincoln Park for the maximum \$50.0 million over the term of the Purchase Agreement, of which Lincoln Park has already purchased \$4.2 million. We obtained stockholder approval to issue up to 3.83 million shares of common stock at the Annual Meeting, so are not constrained by the Nasdaq limit of 19.99% of our outstanding shares that might otherwise apply. However, we will need to seek additional stockholder approval before issuing more than 3.83 million shares. We are not required or permitted to issue any shares of common stock under the Purchase Agreement if such issuance would breach our obligations under the rules or regulations of The Nasdaq Stock Market. In addition, Lincoln Park will not be required to purchase any shares of our common stock if such sale would result in Lincoln Park's beneficial ownership exceeding 4.99% of the then outstanding shares of our common stock. Our inability to access a portion or the full amount available under the Purchase Agreement, in the absence of any other financing sources, could have a material adverse effect on our business.

The extent we rely on Lincoln Park as a source of funding will depend on a number of factors, including the prevailing market price of our common stock and the extent to which we are able to secure working capital from other sources. If obtaining sufficient funding from Lincoln Park were to prove unavailable or prohibitively dilutive, we will need to secure another source of funding in order to satisfy our working capital needs. Even if we sell the remaining \$45.8 million of shares of our common stock remaining available for sale under the Purchase Agreement to Lincoln Park as of November 8, 2023, we may still need additional capital to finance our future production plans and working capital needs, and we may have to raise funds through the issuance of equity or debt securities. Assuming a purchase price of \$1.59 (which represents the closing price of our common stock on November 8, 2023), and that no Additional Commitment Shares are issued, the purchase by Lincoln Park of the entire 1,300,000 shares being registered hereunder and the 1,423,319 shares of our common stock registered under the August 2023 Registration Statement and remaining available to be sold as of November 8, 2023, that are available for purchase pursuant to the Purchase Agreement would result in gross proceeds to us of only approximately \$4.3 million, which would result in a remaining \$41.5 million available under the Purchase Agreement.

Depending on the type and the terms of any financing we pursue, stockholders' rights and the value of their investment in our common stock could be reduced. A financing could involve one or more types of securities including common stock, convertible debt or warrants to acquire common stock. These securities could be issued at or below the then prevailing market price for our common stock. In addition, if we issue secured debt securities, the holders of the debt would have a claim to our assets that would be prior to the rights of stockholders until the debt is paid. Interest on these debt securities would increase costs and negatively impact operating results. If the issuance of new securities results in diminished rights to holders of our common stock, the market price of our common stock could be negatively impacted.

Should the financing we require to sustain our working capital needs be unavailable or prohibitively expensive when we require it, the consequences could be a material adverse effect on our business, operating results, financial condition and prospects.

Our management has broad discretion over the use of the net proceeds from our sale of shares of common stock to Lincoln Park, you may not agree with how we use the proceeds and the proceeds may not be invested successfully.

Our management has broad discretion as to the use of the net proceeds from our sale of shares of common stock to Lincoln Park, and we could use them for purposes other than those currently contemplated. Accordingly, you rely on the judgment of our management with regard to the use of those net proceeds, and you do not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. It is possible that we may invest those net proceeds in a way that does not yield a favorable, or any, return for us. The failure of our management to use such funds effectively could have a material adverse effect on our business, financial condition, operating results and cash flows.

Our stockholders may experience substantial dilution in the value of their investment if we issue additional shares of our capital stock, including in connection with the sale or issuance of our common stock to Lincoln Park, the sale of the shares of common stock acquired by Lincoln Park, and the sale of our common stock by Canaccord. Further, sales of our common stock, or the perception that such sales may occur, could cause the price of our common stock to decline.

We may ultimately decide to sell to Lincoln Park all, some, or no additional shares of our common stock that may be available for us to sell pursuant to the Purchase Agreement. The purchase price for the shares that we may sell to Lincoln Park under the Purchase Agreement will fluctuate based on the price of our common stock. Depending on market liquidity at the time, sales of such shares may cause the trading price of our common stock to fall. If and when we do sell shares to Lincoln Park, after Lincoln Park has acquired the shares, Lincoln Park may resell all or some of those shares at any time or from time to time in its discretion. Therefore, sales to Lincoln Park by us could result in substantial dilution to the interests of other holders of our common stock. Additionally, the sale of a substantial number of shares of our common stock to Lincoln Park, or the anticipation of such sales, could make it more difficult for us to sell equity or equity-related securities in the future at a time and at a price that we might otherwise wish to effect sales.

Our charter allows us to issue up to 100,000,000 shares of our common stock and to issue and designate the rights of, without stockholder approval, and up to 5,000,000 shares of preferred stock. We will need to raise additional capital in order to initiate or complete additional development activities for all of our product candidates, to pursue additional disease indications for our product candidates, or to finance future strategic investments or acquisitions. This in turn may require us to issue a substantial amount of securities. As a result, we may in the future sell additional shares of our common stock or other securities convertible into or exchangeable for our common stock, including at prices that may be lower than the prices paid by existing stockholders, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders, which could result in substantial dilution to the interests of existing stockholders. There can be no assurance that we will be able to attract the capital needed to execute on our business plan and sustain our operations. Moreover, we cannot predict the size of future issuances of our common stock, as well as securities convertible into or exercisable for common stock, or the effect, if any, that future issuances and sales of our securities will have on the market price of our common stock. A substantial majority of the outstanding shares of our common stock, as well as a substantial majority of the shares of common stock issuable upon exercise of outstanding options, are freely tradable without restriction or further registration under the Securities Act. Sales of substantial amounts of our common stock, as well as securities convertible into or exercisable for common stock, including shares issued in connection with an acquisition or securing funds to complete any clinical trial plans, or the perception that such sales could occur, may result in substantial dilution and may adversely affect prevailing market prices for our common stock.

If we fail to maintain proper and effective internal controls, our ability to produce accurate financial statements on a timely basis could be impaired.

We are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act and the rules and regulations of Nasdaq. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting. We must perform system and process evaluation and testing of our internal control over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting in our Annual Report on Form 10-K and quarterly report on Form 10-Q, as required by Section 404 of the Sarbanes-Oxley Act.

During the quarter ended June 30, 2023, we recognized immaterial grant revenue related to reimbursable development costs incurred in the fourth quarter of 2022 and the first quarter of 2023 that were eligible for revenue recognition in those respective prior periods. These costs were eligible for reimbursement under our CPRIT Grant, but were not correctly recognized in prior period grant revenue due to management's view that insufficient progress had been made in the ReSPECT -LM clinical trial, despite no performance specific

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milestones in the grant outside of a reasonableness test for reimbursement of expenses. Management has concluded that the correction to grant revenue in the prior periods did not cause a material misstatement of our financial statements.

We did not have adequate controls to apply appropriate accounting principles to significant and unusual grant revenue transactions. Specifically, controls over identification of significant and/or unusual transactions requiring technical analysis were not operating effectively. Management evaluated the impact of this deficiency on our disclosure controls and procedures and concluded that the control deficiency represents a material weakness. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of the Company's annual or interim financial statements will not be prevented or detected on a timely basis.

While we will be taking remediation measures, we cannot assure investors that these measures will significantly improve or remediate the material weakness described above.

We may in the future discover additional weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. Our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected.

If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act, or if we are unable to maintain proper and effective internal controls, we may not be able to produce timely and accurate financial statements. If that were to happen, the market price of our common stock could decline and we could be subject to sanctions or investigations by Nasdaq, the SEC or other regulatory authorities.

Furthermore, if our remediation of the material weakness is not effective, or if we experience additional material weaknesses in the future or otherwise fail to maintain an effective system of internal controls in the future, we may not be able to accurately or timely report our financial condition or results of operations, which may adversely affect investor confidence in us and, as a result, the value of our common stock.

FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated herein by reference contain forward-looking statements which are made pursuant to the safe harbor provisions of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Statements other than statements of historical fact, which address activities, events or developments that we “intend,” “expect,” “believe,” “anticipate,” “will,” “should,” “would,” “could,” “may,” “designed,” “potential,” “evaluate,” “progressing,” “proceeding,” “exploring,” “hopes,” and similar expressions, or future conditional verbs such as “will,” “should,” “would,” “could” or “may” occur in the future are forward looking statements. Such statements are based upon certain assumptions and assessments made by our management in light of their experience and their perception of historical trends, current conditions, expected future developments and other factors they believe to be appropriate.

These statements include, without limitation, statements regarding: our anticipated expenditures, including research and development, and general and administrative expenses; our strategic collaborations and license agreements, intellectual property, FDA and EMA approvals and interactions and government regulation; the potential size of the market for our product candidates; our research and development efforts; results from our pre-clinical and clinical studies and the implications of such results regarding the efficacy or safety of our product candidates; the safety profile, pathways, and efficacy of our product candidates and formulations; anticipated advantages of our product candidates over other products available in the market and being developed; the populations that will most benefit from our product candidates and indications that will be pursued with each product candidate; anticipated progress in our current and future clinical trials; plans and strategies to create novel technologies; our IP strategy; future development and/or expansion of our product candidates and therapies in our markets; sources of competition for any of our product candidates; our ability to generate product or development revenues and the sources of such revenue; our ability to effectively manage our gross profit margins; our ability to obtain and maintain regulatory approvals; expectations as to our future performance; portions of the “Liquidity and Capital Resources” section of our annual and quarterly reports filed with the SEC; our ability to fully access our equity line with Lincoln Park; our need for additional financing and the availability thereof; our ability to continue as a going concern; our ability to remain listed on the Nasdaq Capital Market; our ability to repay or refinance some or all of our outstanding indebtedness and our ability to raise capital in the future; our ability to transfer the drug product manufacture to a contract drug manufacturing organization; and the potential enhancement of our cash position through development, marketing, and licensing arrangements.

Our actual results may differ, including materially, from those anticipated in these forward-looking statements as a result of various risks and uncertainties. These risks and uncertainties include, but are not limited to, those risks discussed in this prospectus under “Risk Factors,” the risks described under “Part I—Item 1A—Risk Factors” in our Annual Report on Form 10-K for the year ended December 31, 2022, and under “Part II, Item 1A—Risk Factors” in our Quarterly Reports on Form 10-Q, both of which are incorporated herein by reference. We encourage you to read these risks carefully. We caution you not to place undue reliance on the forward-looking statements contained or incorporated by reference in this prospectus. These forward-looking statements speak only as of the date made. We assume no obligation or undertaking to update any forward-looking statements to reflect any changes in expectations with regard thereto or any change in events, conditions or circumstances on which any such statement is based. You should, however, review additional disclosures we make in the reports we file with the SEC.

SELECTED FINANCIAL DATA REFLECTING REVERSE STOCK SPLIT**Reverse Stock Split**

On May 1, 2023, we effected a 1-for-15 reverse stock split of our common stock. The total number of outstanding shares of capital stock was amended from approximately 37,400,000 to approximately 2,493,333. The par value per common share remained unchanged. The audited consolidated financial statements of Plus Therapeutics, Inc. included in the Annual Report on Form 10-K for the year ended December 31, 2022, and the unaudited condensed consolidated financial statements included in our Quarterly Report on Form 10-Q for the period ended March 31, 2023, which are incorporated by reference into this prospectus are presented without giving effect to the reverse stock split. Except where the context otherwise requires, share numbers in this prospectus reflect the 1-for-15 reverse stock split of our common stock.

The following selected financial data has been derived from our audited consolidated financial statements included in our Annual Report on Form 10-K filed with the SEC on February 23, 2023, and our unaudited condensed consolidated financial statements included in our Quarterly Report on Form 10-Q filed with the SEC on April 20, 2023, as adjusted to reflect the reverse stock split for all periods presented. Our historical results are not indicative of the results that may be expected in the future and results of interim periods are not indicative of the results for the entire year.

AS REPORTED (in thousands, except share and per share amounts):

	Years Ended December 31,	
	2022	2021
Net loss and comprehensive loss	\$ 20,275	\$ 13,399
Net loss per share, basic and diluted	\$ (0.77)	\$ (1.11)
Weighted average common shares outstanding, basic and diluted	26,255,256	12,089,186
Common shares outstanding at year end	33,601,373	15,510,025

	Three Months Ended March 31,	
	2023	2022
		(Unaudited)
Net loss and comprehensive loss	\$ 4,805	\$ 4,116
Net loss per share, basic and diluted	\$ (0.14)	\$ (\$0.19)
Weighted average common shares outstanding, basic and diluted	34,800,260	21,507,061
Common shares outstanding at period end	36,123,833	33,601,373

AS ADJUSTED FOR 1-FOR-15 REVERSE STOCK SPLIT (unaudited, in thousands, except share and per share amounts):

	Years Ended December 31,	
	2022	2021
	(Unaudited)	
Net loss and comprehensive loss	\$ 20,275	\$ 13,399
Net loss per share, basic and diluted	(\$11.58)	(\$16.63)
Weighted average common shares outstanding, basic and diluted	1,750,350	805,945
Common shares outstanding at year end	2,240,091	1,034,001

	Three Months Ended March 31,	
	2023	2022
	(Unaudited)	
Net loss and comprehensive loss	\$ 20,275	\$ 13,399
Net loss per share, basic and diluted	(\$8.74)	(\$9.35)
Weighted average common shares outstanding, basic and diluted	2,320,017	1,433,804
Common shares outstanding at period end	2,408,255	2,240,091

THE LINCOLN PARK TRANSACTION

General

On August 2, 2022, we entered into the Purchase Agreement with Lincoln Park, pursuant to which Lincoln Park has agreed to purchase from us up to an aggregate of \$50.0 million of our common stock (subject to certain limitations) from time to time over the term of the Purchase Agreement. Also on August 2, 2022, we entered into the Registration Rights Agreement pursuant to which we filed with the SEC the registration statement that includes this prospectus to register for resale under the Securities Act the shares of our common stock that have been and may be issued to Lincoln Park under the Purchase Agreement.

This prospectus covers the resale of up to 1,300,000 shares of our common stock that we have reserved for issuance and sale to Lincoln Park under the Purchase Agreement from time to time. Under the 2022 Registration Statement, we registered 633,333 shares of our common stock, comprised of: (i) 32,846 shares of our common stock that we have already issued to Lincoln Park as Initial Commitment Shares for making its irrevocable commitment to purchase our common stock under the Purchase Agreement at our direction, and (ii) up to 600,486 shares that we had reserved for future issuance and sale to Lincoln Park from time to time at our determination. Under the August 2023 Registration Statement, we registered 1,500,000 shares of our common stock that we may issue and sell from time to time, at our sole discretion, to Lincoln Park under the Purchase Agreement. As of November 8, 2023, we had issued and sold an aggregate of 677,167 shares of common stock pursuant to the Purchase Agreement and under the Prior Registration Statements, and 1,423,319 shares of our common stock remained available to be sold under the August 2023 Registration Statement.

We did not have the right to commence sales of our common stock to Lincoln Park under the Purchase Agreement until the Commencement Date. From and after the Commencement Date, we may, from time to time and at our sole discretion for a period of 36 months after the Commencement Date, on any business day that we select on which the closing sale price of our common stock equals or exceeds \$1.00 per share, direct Lincoln Park to purchase in a Regular Purchase up to 6,666 shares of our common stock (or, if higher, such number of shares of our common stock equal to \$150,000), which amount may be increased up to a maximum amount of 20,000 shares depending on the market price of our common stock at the time of sale, subject to a maximum commitment of \$1,000,000 per Regular Purchase. In addition, Lincoln Park has committed to purchase other “accelerated amounts” and/or “additional accelerated amounts” under certain circumstances. We control the timing and amount of any sales of our common stock to Lincoln Park. The purchase price of the shares of our common stock that may be sold to Lincoln Park in Regular Purchases under the Purchase Agreement is based on the market price of our common stock preceding the time of sale as computed under the Purchase Agreement. The purchase price per share will be equitably adjusted as provided in the Purchase Agreement for any reorganization, recapitalization, non-cash dividend, stock split, or other similar transaction as set forth in the Purchase Agreement. We may at any time in our sole discretion terminate the Purchase Agreement without fee, penalty or cost upon one business day notice. There are no restrictions on future financings, rights of first refusal, participation rights, penalties or liquidated damages in the Purchase Agreement or Registration Rights Agreement, other than a prohibition on our entering into certain types of transactions that are defined in the Purchase Agreement as “Variable Rate Transactions.” Lincoln Park may not assign or transfer its rights and obligations under the Purchase Agreement.

As consideration for Lincoln Park’s irrevocable commitment to purchase shares of our common stock upon the terms of and subject to satisfaction of the conditions set forth in the Purchase Agreement, we paid \$125,000 in cash as an Initial Commitment Fee and issued 32,846 Commitment Shares to Lincoln Park in consideration for its commitment to purchase shares of our common stock at our direction under the Purchase Agreement. We have also agreed to pay an Additional Commitment Fee of \$625,000, which we may elect to pay in cash or shares of our common stock or any combination thereof, upon our receipt of \$25.0 million aggregate gross proceeds from sales of common stock to Lincoln Park under the Purchase Agreement. Through November 8, 2023, \$4.2 million of common stock have been sold under the Prior Registration Statements.

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As of September 30, 2023, there were 4,522,656 shares of our common stock outstanding, of which 4,483,177 shares of our common stock were held by non-affiliates. If all of the 1,300,000 shares offered by Lincoln Park under this prospectus were issued and outstanding, such shares would represent approximately 22.3% of the total number of shares of our common stock outstanding and approximately 22.5% of the total number of outstanding shares held by non-affiliates, in each case as of September 30, 2023. If in addition to the shares offered by Lincoln Park under this prospectus, the 1,423,319 shares of our common stock available as of November 8, 2023, to be sold under the August 2023 Registration Statement were issued and outstanding, such shares would represent in the aggregate approximately 37.6% of the total number of shares of our common stock outstanding and approximately 37.8% of the total number of outstanding shares held by non-affiliates, in each case as of September 30, 2023. The Purchase Agreement provides that we may sell up to an aggregate of \$50.0 million of our common stock to Lincoln Park, of which \$45.8 million remains to be sold under the Purchase Agreement. We have filed the registration statement that includes this prospectus so that we may issue to Lincoln Park up to 1,300,000 shares of our common stock from time to time from and after the date of this prospectus through sales under the Purchase Agreement. Depending on the market prices of our common stock at the time we elect to issue and sell such shares to Lincoln Park under the Purchase Agreement, we may need to sell more shares to Lincoln Park than are offered under this prospectus to receive aggregate gross proceeds equal to the \$50.0 million total commitment of Lincoln Park under the Purchase Agreement, in which case we must again register for resale under the Securities Act additional shares of our common stock, which could cause additional substantial dilution to our stockholders. The number of shares ultimately offered for resale by Lincoln Park is dependent upon the number of shares we sell to Lincoln Park under the Purchase Agreement.

Prior to entering into the Purchase Agreement with Lincoln Park, we received stockholder approval at our 2022 Annual Meeting of Stockholders that was held on May 16, 2022 (the “Annual Meeting”) pursuant to Nasdaq Listing Rules 5635(a), 5635(b) and 5635(d) to permit issuances of our common stock (including the issuance of more than 19.99% of our common stock) to Lincoln Park pursuant to the Purchase Agreement. Based on the closing price of our common stock of \$1.00 per share on March 22, 2022 (the lowest closing sale price between January 1, 2022 and the date of the proxy statement filed in connection with the Annual Meeting, as reported on Nasdaq.com, as adjusted for the post-reverse stock split basis), the maximum number of shares we could issue and sell under the Purchase Agreement is approximately 3.83 million shares. Accordingly, we requested and received stockholder approval for the issuance of up to 3.83 million shares of our common stock in the aggregate under the Purchase Agreement. We would seek additional stockholder approval before issuing more than an aggregate of 3.83 million shares under the Purchase Agreement.

The Purchase Agreement also prohibits us from directing Lincoln Park to purchase any shares of common stock if those shares, when aggregated with all other shares then beneficially owned by Lincoln Park and its affiliates, would result in Lincoln Park having beneficial ownership of shares of our common stock, as calculated pursuant to Section 13(d) of the Exchange Act and Rule 13d-3 thereunder, in excess of the Beneficial Ownership Cap at any time.

There are substantial risks to our stockholders as a result of the sale and issuance of common stock to Lincoln Park under the Purchase Agreement. These risks include substantial dilution, significant declines in our stock price and our inability to draw sufficient funds when needed. See “Risk Factors.” The sale of our common stock to Lincoln Park under the Purchase Agreement will not affect the rights or privileges of our other stockholders, except that the economic and voting interests of our existing stockholders will be diluted as a result of any such sale. Although the number of shares of common stock that our other stockholders own will not decrease, the shares of our common stock owned by our other stockholders will represent a smaller percentage of our total outstanding shares after any such sale to Lincoln Park under the Purchase Agreement.

Purchase of Shares of our Common Stock under the Purchase Agreement

Under the Purchase Agreement, so long as the closing sale price of our common stock is not below \$1.00 on a particular Business Day, we may from time to time direct Lincoln Park to purchase up to 6,666 shares of our common stock (or, if higher, such number of shares of our common stock such that the limit equals (or as closely equals without exceeding) \$150,000) in a Regular Purchase on such business day (such share amount limitation, the “Regular Purchase Share Limit”), provided, however, that the

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Regular Purchase may be increased to up to 20,000 shares of our common stock, provided that the closing sale price of our common stock is not below not below certain threshold prices set forth in the Purchase Agreement. In each case, Lincoln Park's maximum commitment in any single Regular Purchase may not exceed \$1,000,000. The Regular Purchase Share Limit is subject to proportionate adjustment in the event of a reorganization, recapitalization, non-cash dividend, stock split or other similar transaction; provided, that if after giving effect to such full proportionate adjustment, the adjusted Regular Purchase Share Limit would preclude us from requiring Lincoln Park to purchase shares of our common stock at an aggregate purchase price equal to or greater than \$150,000 in any single Regular Purchase, then the Regular Purchase Share Limit will not be fully adjusted, but rather the Regular Purchase Share Limit for such Regular Purchase shall be adjusted as specified in the Purchase Agreement, such that, after giving effect to such adjustment, the Regular Purchase Share Limit will be equal to (or as close as can be derived from such adjustment without exceeding) \$150,000.

The purchase price per share for each such Regular Purchase will be equal to the lower of:

- the lowest sale price for our common stock on the purchase date for such shares of our common stock; and
- the arithmetic average of the three lowest closing sale prices for our common stock during the 10 consecutive business days ending on the business day immediately preceding the purchase date of such shares of our common stock.

In addition to Regular Purchases described above, we may also direct Lincoln Park, on any business day on which we have properly submitted a Regular Purchase notice directing Lincoln Park to purchase the maximum number of shares of our common stock that we are then permitted to include in a single Regular Purchase notice, to purchase an additional amount of our common stock, which we refer to as an Accelerated Purchase, not to exceed the lesser of:

- 30% of the aggregate number of shares of our common stock traded during all or, if certain trading volume or market price thresholds specified in the Purchase Agreement are crossed on the applicable Accelerated Purchase date, which is defined as the next business day following the purchase date for the corresponding Regular Purchase, the portion of the normal trading hours on the applicable Accelerated Purchase date prior to such time that any one of such thresholds is crossed, which period of time on the applicable Accelerated Purchase date we refer to as the Accelerated Purchase Measurement Period; and
- 300% of the number of purchase shares purchased pursuant to the corresponding Regular Purchase.

The purchase price per share for each such Accelerated Purchase will be equal to 96.5% of the lower of:

- the volume weighted average price of our common stock during the Accelerated Purchase Measurement Period on the applicable Accelerated Purchase date; and
- the closing sale price of our common stock on the applicable Accelerated Purchase date.

We may also direct Lincoln Park, not later than 1:00 p.m., Eastern time, on a business day on which an Accelerated Purchase has been completed and all of the shares of our common stock to be purchased thereunder (and under the corresponding Regular Purchase) have been properly delivered to Lincoln Park in accordance with the Purchase Agreement prior to such time on such business day, to purchase an additional amount of our common stock, which we refer to as an Additional Accelerated Purchase, of up to the lesser of:

- 30% of the aggregate number of shares of our common stock traded during a certain portion of the normal trading hours on such Accelerated Purchase date as determined in accordance with the Purchase Agreement, which period of time we refer to as the Additional Accelerated Purchase Measurement Period; and

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- 300% of the number of purchase shares purchased pursuant to the Regular Purchase corresponding to the Accelerated Purchase that was completed on such Accelerated Purchase date on which an Additional Accelerated Purchase notice was properly received.

We may, in our sole discretion, submit multiple Additional Accelerated Purchase notices to Lincoln Park prior to 1:00 p.m., Eastern time, on a single Accelerated Purchase date, provided that all prior Accelerated Purchases and Additional Accelerated Purchases (including those that have occurred earlier on the same day) have been completed and all of the shares of our common stock to be purchased thereunder (and under the corresponding Regular Purchase) have been properly delivered to Lincoln Park in accordance with the Purchase Agreement.

The purchase price per share for each such Additional Accelerated Purchase will be equal to 96.5% of the lower of:

- the volume weighted average price of our common stock during the applicable Additional Accelerated Purchase Measurement Period on the applicable Additional Accelerated Purchase date; and
- the closing sale price of our common stock on the applicable Additional Accelerated Purchase date.

In the case of Regular Purchases, Accelerated Purchases and Additional Accelerated Purchases, the purchase price per share will be equitably adjusted for any reorganization, recapitalization, non-cash dividend, stock split, reverse stock split or other similar transaction occurring during the business days used to compute the purchase price.

Other than as described above, there are no trading volume requirements or restrictions under the Purchase Agreement, and we will control the timing and amount of any sales of our common stock to Lincoln Park.

Minimum Share Price

Under the Purchase Agreement, we and Lincoln Park may not effect any sales of shares of our common stock under the Purchase Agreement on any purchase date that the closing sale price of our common stock is less than the floor price of \$1.00 per share of common stock, which will be appropriately adjusted for any reorganization, recapitalization, non-cash dividend, stock split or other similar transaction. Upon consummation of any such reorganization, recapitalization, non-cash dividend, stock split or other similar transaction, the adjusted floor price per share of common stock will be the lower of (i) the adjusted price and (ii) \$1.00.

Events of Default

Events of default under the Purchase Agreement include the following:

- The effectiveness of the registration statement of which this prospectus forms a part lapses for any reason (including, without limitation, the issuance of a stop order), or any required prospectus supplement and accompanying prospectus are unavailable for the resale by Lincoln Park of our common stock offered hereby, and such lapse or unavailability continues for a period of 10 consecutive business days or for more than an aggregate of 30 business days in any 365-day period.
- Suspension by our principal market of our common stock from trading for a period of one business day.
- The de-listing of our common stock from the Nasdaq Capital Market, our principal market, provided our common stock is not immediately thereafter trading on the New York Stock Exchange, the Nasdaq Capital Market, the Nasdaq Global Market, the Nasdaq Global Select Market, the NYSE American, the NYSE Arca, or the OTCQX Best Market or the OTCQB Venture Market operated by OTC Markets Group Inc. (or nationally recognized successor thereto). See the discussion about compliance with Nasdaq listing standards at the bottom of this subsection “—Events of Default.”

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- The failure of our transfer agent to issue to Lincoln Park shares of our common stock within two business days after the applicable date on which Lincoln Park is entitled to receive such shares of our common stock.
- Any breach of the representations or warranties or covenants contained in the Purchase Agreement or Registration Rights Agreement that has or could have a material adverse effect on us and, in the case of a breach of a covenant that is reasonably curable, that is not cured within five business days.
- Any voluntary or involuntary participation or threatened participation in insolvency or bankruptcy proceedings by or against us.
- If at any time we are not eligible to transfer our common stock electronically.
- If at any time the Exchange Cap (to the extent applicable under the terms of the Purchase Agreement) is reached and our stockholders have not approved the issuance of common stock in excess of the Exchange Cap in accordance with applicable Nasdaq rules.

Lincoln Park does not have the right to terminate the Purchase Agreement upon any of the events of default set forth above, although the Purchase Agreement would automatically terminate in the event of any voluntary or involuntary participation or threatened participation in insolvency or bankruptcy proceedings by or against us. During an event of default, all of which are outside of Lincoln Park's control, we may not direct Lincoln Park to purchase any shares of our common stock under the Purchase Agreement.

On May 24, 2022, we received notice from The Nasdaq Stock Market that because the closing bid price for our common stock had fallen below \$1.00 per share for 30 consecutive business days, we no longer complied with the minimum bid price requirement pursuant to Nasdaq Listing Rule 5550(a)(2) (the "Minimum Bid Requirement"). The notice had no immediate effect on the listing or trading of our common stock. Pursuant to Nasdaq Listing Rule 5810(c)(3)(A), as we were provided an initial compliance period of 180 calendar days, or until November 21, 2022, to regain compliance with the Minimum Bid Requirement. To regain compliance, the closing bid price of our common stock must meet or exceed \$1.00 per share for a minimum of 10 consecutive business days. Because we did not achieve compliance with the Minimum Bid Requirement by November 21, 2022, we were eligible and received an additional 180 calendar days to regain compliance. On May 1, 2023, we effected a reverse stock split of 15-for-1, and the closing bid price of our common stock increased. On May 15, 2023, we received written notice from Nasdaq that we had regained compliance with the minimum bid price requirement.

Our Termination Rights

We have the unconditional right, at any time, for any reason and without any payment or liability to us, to give notice to Lincoln Park to terminate the Purchase Agreement.

No Short-Selling or Hedging by Lincoln Park

Lincoln Park has agreed that neither it nor any of its affiliates shall engage in any direct or indirect short-selling or hedging of our common stock during any time prior to the termination of the Purchase Agreement.

Prohibitions on Variable Rate Transactions

There are no restrictions on future financings, rights of first refusal, participation rights, penalties or liquidated damages in the Purchase Agreement or Registration Rights Agreement other than a prohibition on entering into a "Variable Rate Transaction," as defined in the Purchase Agreement.

Effect of Performance of the Purchase Agreement on Our Stockholders

All 1,300,000 shares of our common stock being registered for resale in this offering that may be sold or have been sold by us to Lincoln Park under the Purchase Agreement are expected to be freely tradable. It is

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anticipated that shares registered for resale in this offering will be sold at our sole discretion from time to time from and after the date of this prospectus for a period of 36 months after the Commencement Date. The sale by Lincoln Park of a significant amount of shares of our common stock registered in this offering at any given time could cause the market price of our common stock to decline and to be highly volatile. Sales of our common stock to Lincoln Park, if any, will depend upon market conditions, the trading price of our common stock, determinations by us as to the appropriate source of funding for our company and its operations and other factors to be determined by us. We may ultimately decide to sell to Lincoln Park all, some or none of the shares of our common stock that may be available for us to sell pursuant to the Purchase Agreement. If and when we do sell shares of our common stock to Lincoln Park, after Lincoln Park has acquired the shares of our common stock, Lincoln Park may resell all, some or none of those shares of our common stock at any time or from time to time in its discretion. Therefore, sales to Lincoln Park by us under the Purchase Agreement may result in substantial dilution to the interests of other holders of our common stock. In addition, if we sell a substantial number of shares of our common stock to Lincoln Park under the Purchase Agreement, or if investors expect that we will do so, the actual sales of shares of our common stock or the mere existence of our arrangement with Lincoln Park may make it more difficult for us to sell equity or equity-related securities in the future at a time and at a price that we might otherwise wish to effect such sales. However, we have the right to control the timing and amount of any sales of our common stock to Lincoln Park and the Purchase Agreement may be terminated by us at any time without any cost to us.

Pursuant to the terms of the Purchase Agreement, we have the right, but not the obligation, from time to time to direct Lincoln Park to purchase up to \$50.0 million of our common stock, of which \$45.8 million remains to be purchased under the Purchase Agreement (exclusive of the 32,846 Commitment Shares issued to Lincoln Park). Depending on the price per share at which we sell our common stock to Lincoln Park pursuant to the Purchase Agreement, we may need to sell to Lincoln Park more shares of our common stock than are offered under this prospectus in order to receive aggregate gross proceeds equal to the approximately \$45.8 million remaining balance of the \$50.0 million total commitment available to us under the Purchase Agreement. If we choose to do so, we must again register for resale under the Securities Act such additional shares of our common stock, which could cause additional substantial dilution to our stockholders. The number of shares ultimately offered for resale by Lincoln Park under this prospectus is dependent upon the number of shares we direct Lincoln Park to purchase under the Purchase Agreement.

Prior to entering into the Purchase Agreement with Lincoln Park, we received stockholder approval at our Annual Meeting pursuant to Nasdaq Listing Rules 5635(a), 5635(b) and 5635(d) to permit issuances of our common stock (including the issuance of more than 19.99% of our common stock) to Lincoln Park pursuant to the Purchase Agreement. Based on the closing price of our common stock of \$1.00 per share on March 22, 2022 (the lowest closing sale price between January 1, 2022 and the date of the proxy statement filed in connection with the Annual Meeting, as reported on Nasdaq.com), the maximum number of shares we could issue and sell under the Purchase Agreement is approximately 3.83 million shares. Accordingly, we requested and received stockholder approval for the issuance of up to 3.83 million shares of our common stock in the aggregate under the Purchase Agreement. We would seek additional stockholder approval before issuing more than an aggregate of 3.83 million shares under the Purchase Agreement.

We have filed the registration statement that includes this prospectus so that we may issue to Lincoln Park up to 1,300,000 shares of our common stock from time to time from and after the date of this prospectus through sales under the Purchase Agreement. The following table sets forth the amount of gross proceeds we may receive from Lincoln Park from our sale of up to 1,300,000 shares of our common stock that we may issue and sell to

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Lincoln Park in the future under the Purchase Agreement assuming that all such common stock is sold at varying purchase prices designated below:

Assumed Average Purchase Price Per Share	Number of shares to be Issued if Full Purchase(1)	Percentage of Outstanding Shares of Common Stock After Giving Effect to the Sales to Lincoln Park(2)	Gross Proceeds from the Future Sale of Shares to Lincoln Park Under the Purchase Agreement(1)
\$1.34	1,300,000	22.3%	\$ 1,742,000
\$1.59(3)	1,300,000	22.3%	\$ 2,067,000
\$1.84	1,300,000	22.3%	\$ 2,392,000
\$2.09	1,300,000	22.3%	\$ 2,717,000

- (1) Although the Purchase Agreement provides that we may sell up to \$50.0 million of our common stock to Lincoln Park, we are only registering 1,300,000 shares of our common stock for resale under the registration statement of which this prospectus is a part, which may or may not cover all the shares of our common stock we ultimately sell to Lincoln Park under the Purchase Agreement, depending on the purchase price per share.
- (2) The denominator is based on 4,522,656 shares of our common stock outstanding as of September 30, 2023, adjusted to include the number of shares set forth in the adjacent column which we would have sold to Lincoln Park, assuming the purchase price in the adjacent column. The numerator is based on the number of shares issuable under the Purchase Agreement at the corresponding assumed purchase price set forth in the adjacent column, without giving effect to the Beneficial Ownership Cap.
- (3) The closing sale price per share of our common stock on November 8, 2023.

USE OF PROCEEDS

This prospectus relates to shares of our common stock that may be offered and sold from time to time by Lincoln Park. We will receive no proceeds from the sale of shares of common stock by Lincoln Park in this offering. We may receive up to \$50.0 million in aggregate gross proceeds under the Purchase Agreement, of which \$45.8 million remains to be purchased, from any sales we make to Lincoln Park pursuant to the Purchase Agreement. Assuming a purchase price of \$1.59 (which represents the closing price of our common stock on November 8, 2023), the purchase by Lincoln Park of the entire 1,300,000 shares being registered for resale hereunder, which we have the right but not the obligation to sell to Lincoln Park, would result in gross proceeds to us of approximately \$2.1 million, and we estimate approximately \$2.0 million of net proceeds, after estimated fees and expenses. See “Plan of Distribution” elsewhere in this prospectus for more information.

We expect to use any proceeds that we receive under the Purchase Agreement for working capital and general corporate purposes. The amounts and timing of these expenditures will depend on a number of factors, such as the timing and progress of our research and development efforts, regulatory actions affecting our product candidates and our business, technological advances and the competitive environment for our product candidates. As we are unable to predict the timing or amount of potential issuances of all of the shares being registered hereunder that are issuable to the Purchase Agreement, we cannot specify with certainty all of the particular uses for the net proceeds that we will have from the sale of such shares. Accordingly, our management will have broad discretion in the application of the net proceeds. We may also use a portion of the net proceeds to acquire or invest in complementary businesses, technologies, product candidates or other intellectual property, although we have no present commitments or agreements to do so. We may use the proceeds for purposes that are not contemplated at the time of this offering. Pending use of the net proceeds as described above, we expect to invest the net proceeds in short- and intermediate-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government. It is possible that no shares will be issued under the Purchase Agreement.

DILUTION

The sale of our common stock to Lincoln Park pursuant to the Purchase Agreement will have a dilutive impact on our stockholders. In addition, the lower our stock price is at the time we exercise our right to sell shares to Lincoln Park, the more shares of our common stock we will have to issue to Lincoln Park pursuant to the Purchase Agreement and our existing stockholders would experience greater dilution.

After giving effect to the assumed sale of 1,300,000 shares of our common stock to Lincoln Park pursuant to the Purchase Agreement at an assumed sale price of \$1.59 per share of our common stock (which represents the closing price of our common stock on November 8, 2023) and after deducting estimated offering expenses payable by us, our as-adjusted net tangible book value as of September 30, 2023 would have been approximately \$4.2 million, or \$0.72 per share. This represents an immediate increase in net tangible book value of \$0.23 per share to existing stockholders and an immediate dilution of \$0.87 per share to new investors. The table below illustrates this per share dilution:

Assumed offering price per share	\$1.59
Historical net tangible book value per share as of September 30, 2023	\$0.49
Increase per share attributable to this offering	<u>\$0.23</u>
As adjusted net tangible book value per share after this offering	<u>\$0.72</u>
Dilution per share to new investors	<u>\$0.87</u>

The number of shares of common stock to be outstanding immediately after this offering in the table above is based on 4,522,656 shares outstanding as of September 30, 2023 and excludes, as of September 30, 2023:

- 78,334 shares of common stock issuable upon exercise of stock options outstanding under our equity incentive plans, with a weighted-average exercise price of \$68.10 per share;
- 6,023 shares of common stock reserved for future issuance under our 2015 New Employee Incentive Plan;
- 179,640 shares of common stock reserved for future issuance under our 2020 Stock Incentive Plan;
- 398 and 27,792 shares of common stock issuable upon conversion of 1,014 shares of Series B Convertible Preferred Stock and 938 shares of Series C Preferred Stock, respectively;
- 142,733 shares of common stock issuable upon the exercise of warrants to purchase common stock, with a weighted-average exercise price of \$34.10 per share; and
- up to 1,423,319 shares of our common stock available to be sold as of November 8, 2023, pursuant to the Purchase Agreement under the August 2023 Registration Statement.

THE SELLING STOCKHOLDER

This prospectus relates to the possible resale by the selling stockholder, Lincoln Park, of shares of our common stock that have been and may be issued to Lincoln Park pursuant to the Purchase Agreement. We are filing the registration statement that includes this prospectus pursuant to the provisions of the Registration Rights Agreement, which we entered into with Lincoln Park on August 2, 2022, concurrently with our execution of the Purchase Agreement, in which we agreed to provide certain registration rights with respect to sales by Lincoln Park of the shares of our common stock that have been and may be issued to Lincoln Park under the Purchase Agreement.

Lincoln Park, as the selling stockholder, may, from time to time, offer and sell pursuant to this prospectus up to 1,300,000 shares of our common stock that we may have issued or may sell to Lincoln Park under the Purchase Agreement. The selling stockholder may sell some, all, or none of its shares of common stock. We do not know how long the selling stockholder will hold the shares of our common stock before selling them, and we currently have no agreements, arrangements or understandings with the selling stockholder regarding the sale of any of the shares of common stock. See “Plan of Distribution”.

The table below sets forth, to our knowledge, information concerning the beneficial ownership of shares of our common stock by the selling stockholder as of September 30, 2023. The percentages of shares owned before and after the offering are based on 4,522,656 shares of our common stock outstanding as of September 30, 2023. The information in the table below with respect to the selling stockholder has been obtained from the selling stockholder.

Beneficial ownership is determined in accordance with the rules of the SEC and includes voting or investment power with respect to shares. Unless otherwise indicated below, to our knowledge, all persons named in the table have sole voting and investment power with respect to their shares of common stock. The inclusion of any shares in this table does not constitute an admission of beneficial ownership for the person named below.

Throughout this prospectus, when we refer to the shares of common stock being offered for resale by the selling stockholder through this prospectus, we are referring to the shares of common stock that have been and may be issued and sold by us to Lincoln Park pursuant to the Purchase Agreement, unless otherwise indicated.

Name of Selling Stockholder	Number of Shares of Common Stock Owned Prior to Offering(2)		Maximum Number of Shares of Common Stock to be Offered Pursuant to this Prospectus(3)	Number of Shares of Common Stock Owned After Offering	
	Number	Percent		Number	Percent
Lincoln Park Capital Fund, LLC ⁽¹⁾	80,000	1.77%	1,300,000	80,000	1.37%

- (1) Josh Scheinfeld and Jonathan Cope, the Managing Members of Lincoln Park Capital, LLC, the manager of Lincoln Park Capital Fund, LLC, are deemed to be beneficial owners of all of the shares of Class A common stock owned directly by Lincoln Park Capital Fund, LLC. Messrs. Cope and Scheinfeld have shared voting and investment power over the shares of Class A common stock being offered under the registration statement filed with the SEC in connection with the transactions contemplated under the Purchase Agreement and the Registration Rights Agreement. Neither Lincoln Park Capital, LLC nor Lincoln Park Capital Fund, LLC is a licensed broker dealer or an affiliate of a licensed broker dealer.
- (2) In accordance with Rule 13d-3(d) under the Exchange Act, we have excluded from the number of shares of our common stock beneficially owned prior to the offering (i) all of the shares of our common stock that we may issue and sell to Lincoln Park pursuant to the Purchase Agreement that are being registered for resale under the registration statement that includes this prospectus, because the issuance and sale of such shares to

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Lincoln Park under the Purchase Agreement is solely at our discretion and is subject to certain conditions, the satisfaction of all of which are outside of Lincoln Park's control, including the registration statement that includes this prospectus becoming and remaining effective under the Securities Act, and (ii) any Additional Commitment Shares, none of which are being registered for resale hereunder, because such Additional Commitment Shares are only issuable to Lincoln Park if we elect to pay some or all of the \$625,000 additional commitment fee, which will only become payable if and when we receive \$25.0 million aggregate gross proceeds from sales of common stock to Lincoln Park under the Purchase Agreement, in shares of our common stock. The 80,000 shares listed as beneficially owned represent shares purchased under the Purchase Agreement, the resale of which is covered by the Prior Registration Statements, not this Registration Statement. Furthermore, under the terms of the Purchase Agreement, issuances and sales of shares of our common stock to Lincoln Park under the Purchase Agreement are subject to certain limitations on the amounts we may sell to Lincoln Park at any time, including the Beneficial Ownership Cap.

- (3) Although the Purchase Agreement provides that we may sell up to \$50.0 million of our common stock to Lincoln Park, we are only registering 1,300,000 shares of our common stock for resale under this prospectus. Depending on the price per share at which we sell our common stock to Lincoln Park pursuant to the Purchase Agreement, we may need to sell to Lincoln Park under the Purchase Agreement more shares of our common stock than are offered under this prospectus in order to receive aggregate gross proceeds equal to the full \$50.0 million available to us under the Purchase Agreement. If we choose to do so, we must again register for resale under the Securities Act such additional shares. The number of shares ultimately offered for resale by Lincoln Park is dependent upon the number of shares we sell to Lincoln Park under the Purchase Agreement.

MARKET PRICE OF OUR COMMON STOCK AND RELATED STOCKHOLDER MATTERS

Market Information

Our common stock is traded on the Nasdaq Capital Market under the symbol “PSTV.”

Holders

As of November 10, 2023, there were approximately 3 registered holders of our common stock. This number does not include stockholders for whom shares were held in “nominee” or “street name.”

Dividend Policy

We have never declared or paid any cash dividends on our common stock and we do not intend to pay cash dividends in the foreseeable future. We currently expect to retain any future earnings to fund the operation and expansion of our business.

DESCRIPTION OF CAPITAL STOCK

This section describes the general terms and provisions of the shares of our common stock, par value \$0.001 per share, and preferred stock, par value \$0.001 per share, and some of the provisions of our certificate of incorporation and bylaws and of the Delaware General Corporation Law (the "DGCL"). This description is only a summary. Our amended and restated certificate of incorporation, as amended, and our amended and restated bylaws have been filed as exhibits to our periodic reports filed with the SEC, which are incorporated by reference in this prospectus. You should read our amended and restated certificate of incorporation and our amended and restated bylaws for additional information before you buy any of our common stock, preferred stock or other securities. See "Where You Can Find More Information."

Common Stock

We are authorized to issue 100,000,000 shares of common stock. As of September 30, 2023, there were 4,522,656 shares of common stock issued and outstanding. Each holder of common stock is entitled to one vote for each share of common stock held on all matters submitted to a vote of stockholders. We have not provided for cumulative voting for the election of directors in our amended and restated certificate of incorporation, as amended. This means that the holders of a majority of the shares voted can elect all of the directors then standing for election. Subject to preferences that may apply to shares of preferred stock outstanding at the time, the holders of outstanding shares of our common stock are entitled to receive dividends out of assets legally available at the times and in the amounts that our board of directors may determine from time to time. Upon our liquidation, dissolution or winding-up, the holders of common stock are entitled to share ratably in all assets remaining after payment of all liabilities and the liquidation preferences of any outstanding preferred stock. Holders of common stock have no preemptive or conversion rights or other subscription rights. There are no redemption or sinking fund provisions applicable to the common stock. All outstanding shares of common stock are fully paid and nonassessable, and the shares of common stock offered, when issued, will be fully paid and nonassessable.

Preferred Stock

We are authorized to issue 5,000,000 shares of preferred stock, 1,952 shares of which were issued and outstanding as of September 30, 2023. Of this amount, (i) 13,500 shares have been designated Series A Convertible Preferred Stock, 0 shares of which are outstanding, (ii) 10,000 shares have been designated Series B Convertible Preferred Stock, 1,014 shares of which are outstanding, (iii) 7,000 shares have been designated Series C Convertible Preferred Stock, 938 shares of which are outstanding and (iv) 1 share has been designated Series F Preferred Stock, of which no share is outstanding, in each case, as of June 30, 2023.

We may issue additional shares of preferred stock, in series, with such designations, powers, preferences and other rights and qualifications, limitations or restrictions as our board of directors may authorize, without further action by our stockholders, including:

- the distinctive designation of each series and the number of shares that will constitute the series;
- the voting rights, if any, of shares of the series and the terms and conditions of the voting rights;
- the dividend rate on the shares of the series, the dates on which dividends are payable, any restriction, limitation or condition upon the payment of dividends, whether dividends will be cumulative, and the dates from and after which dividends shall accumulate;
- the prices at which, and the terms and conditions on which, the shares of the series may be redeemed, if the shares are redeemable;
- the terms and conditions of a sinking or purchase fund for the purchase or redemption of shares of the series, if such a fund is provided;

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- any preferential amount payable upon shares of the series in the event of the liquidation, dissolution or winding up of, or upon the distribution of any of our assets; and
- the prices or rates of conversion or exchange at which, and the terms and conditions on which, the shares of the series may be converted or exchanged into other securities, if the shares are convertible or exchangeable.

The particular terms of any additional series of preferred stock, and the transfer agent and registrar for that series, will be described in a prospectus supplement. Any material United States federal income tax consequences and other special considerations with respect to any preferred stock offered under this prospectus will also be described in the applicable prospectus supplement.

The issuance of preferred stock could decrease the amount of earnings and assets available for distribution to holders of our common stock or adversely affect the rights and powers, including voting rights, of the holders of our common stock. The issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of our company, which could depress the market price of our common stock.

Series B Preferred Stock

Conversion. Each share of Series B Preferred Stock is convertible, at our option or at the option of the holder at any time, into the number of shares of our common stock determined by dividing the \$1,000 stated value per share of the Series B Preferred Stock by a conversion price of \$2,547.74 per share. In addition, the conversion price per share is subject to adjustment for stock dividends, distributions, subdivisions, combinations or reclassifications. Subject to limited exceptions, a holder of the Series B Preferred Stock will not have the right to convert any portion of the Series B Preferred Stock to the extent that, after giving effect to the conversion, the holder, together with its affiliates, would beneficially own in excess of 9.99% of the number of shares of our common stock outstanding immediately after giving effect to its conversion.

Fundamental Transactions. In the event we effect certain mergers, consolidations, sales of substantially all of our assets, tender or exchange offers, reclassifications or share exchanges in which our common stock is effectively converted into or exchanged for other securities, cash or property, we consummate a business combination in which another person acquires 50% of the outstanding shares of our common stock, or any person or group becomes the beneficial owner of 50% of the aggregate ordinary voting power represented by our issued and outstanding common stock, then, upon any subsequent conversion of the Series B Preferred Stock, a holder of the Series B Preferred Stock will have the right to receive any shares of the acquiring corporation or other consideration it would have been entitled to receive if it had been a holder of the number of shares of common stock then issuable upon conversion in full of the Series B Preferred Stock.

Dividends. Holders of Series B Preferred Stock are entitled to receive dividends (on an as-if-converted-to-common-stock basis) in the same form as dividends actually paid on shares of the common stock when, as and if such dividends are paid on shares of common stock.

Voting Rights. Except as otherwise provided in the certificate of designation for the Series B Preferred Stock or as otherwise required by law, the Series B Preferred Stock has no voting rights.

Liquidation Preference. Upon our liquidation, dissolution or winding-up, whether voluntary or involuntary, holders of Series B Preferred Stock will be entitled to receive out of our assets, whether capital or surplus, an amount equal to the \$1,000 stated value per share for each share of Series B Preferred Stock before any distribution or payment shall be made to the holders of any junior securities.

Redemption Rights. We are not obligated to redeem or repurchase any shares of Series B Preferred Stock. Shares of Series B Preferred Stock are not otherwise entitled to any redemption rights, or mandatory sinking fund or analogous fund provisions.

Series C Preferred Stock

Conversion. Each share of Series C Preferred Stock is convertible, at our option at any time, subject to certain conditions, or at the option of the holder at any time, into the number of shares of our common stock determined by dividing the \$1,000 stated value per share of the Series C Preferred Stock by a conversion price of \$33.75. In addition, the conversion price per share is subject to adjustment for stock dividends, distributions, subdivisions, combinations or reclassifications. Subject to limited exceptions, a holder of the Series C Preferred Stock does not have the right to convert any portion of the Series C Preferred Stock to the extent that, after giving effect to the conversion, the holder, together with its affiliates, would beneficially own in excess of 9.99% of the number of shares of our common stock outstanding immediately after giving effect to its conversion.

Anti-Dilution. Subject to certain exceptions contained in the certificate of designation for the Series C Preferred Stock, including our ability to issue securities in connection with equity awards to service providers, strategic transactions, debt financings, research and development partnerships, an equity line of credit, our “at the market” equity offering program and other customary exceptions, if we issue or sell, or are deemed to have issued or sold, any shares of common stock or Common Stock Equivalents (as defined in the certificate of designation) for a consideration per share lower than the conversion price of the Series C Preferred Stock in effect immediately prior to such issuance or sale, or deemed issuance or sale, then the conversion price of the Series C Preferred Stock then in effect will be reduced to an amount equal to such lower price pursuant to the terms of the certificate of designation.

Fundamental Transactions. In the event we effect certain mergers, consolidations, sales of substantially all of our assets, tender or exchange offers, reclassifications or share exchanges in which our common stock is effectively converted into or exchanged for other securities, cash or property, we consummate a business combination in which another person acquires 50% of the outstanding shares of our common stock, or any person or group becomes the beneficial owner of 50% of the aggregate ordinary voting power represented by our issued and outstanding common stock, then, upon any subsequent conversion of the Series C Preferred Stock, a holder of the Series C Preferred Stock will have the right to receive any shares of the acquiring corporation or other consideration it would have been entitled to receive if it had been a holder of the number of shares of common stock then issuable upon conversion in full of the Series C Preferred Stock.

Dividends. Holders of Series C Preferred Stock are entitled to receive dividends (on an as-if-converted-to-common-stock basis) in the same form as dividends actually paid on shares of the common stock when, as and if such dividends are paid on shares of common stock.

Voting Rights. Except as otherwise provided in the certificate of designation for the Series C Preferred Stock or as otherwise required by law, the Series C Preferred Stock has no voting rights.

Liquidation Preference. Upon our liquidation, dissolution or winding-up, whether voluntary or involuntary, holders of Series C Preferred Stock will be entitled to receive out of our assets, whether capital or surplus, an amount equal to the \$1,000 stated value per share for each share of Series C Preferred Stock before any distribution or payment shall be made to the holders of any junior securities.

Redemption Rights. We are not obligated to redeem or repurchase any shares of Series C Preferred Stock. Shares of Series C Preferred Stock are not otherwise entitled to any redemption rights, or mandatory sinking fund or analogous fund provisions.

Anti-Takeover Effects of Delaware Law and Our Certificate of Incorporation and Bylaws

Certain provisions of Delaware law, our amended and restated certificate of incorporation, as amended, and our amended and restated bylaws could have the effect of delaying, deferring or discouraging another party from acquiring control of us. These provisions, which are summarized below, are expected to discourage certain types of coercive takeover practices and inadequate takeover bids. These provisions are also designed, in part, to encourage persons seeking to acquire control of us to first negotiate with our board of directors.

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Certificate of Incorporation and Bylaws. Our amended and restated certificate of incorporation, as amended, and amended and restated bylaws include provisions that:

- authorize the board of directors to issue, without stockholder approval, blank-check preferred stock with such designations, powers, preferences and other rights and qualifications, limitations or restrictions as our board of directors may authorize, which preferred stock could decrease the amount of earnings and assets available for distribution to holders of our common stock or adversely affect the rights and powers, including voting rights, of the holders of our common stock;
- establish advance notice requirements for stockholder nominations of directors and for stockholder proposals that can be acted on at stockholder meetings;
- limit who may call stockholder meetings;
- require that any action to be taken by our stockholders be effected at a duly called annual or special meeting and not by written consent;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even if less than a quorum; and
- authorize us to indemnify officers and directors against losses that they may incur in investigations and legal proceedings resulting from their services to us, which may include services in connection with takeover defense measures.

Delaware anti-takeover statute. We are subject to the provisions of Section 203 of the DGCL regulating corporate takeovers. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging, under certain circumstances, in a business combination with an interested stockholder for a period of three years following the date the person became an interested stockholder unless:

- prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder; or
- upon completion of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, but not the outstanding voting stock owned by the interested stockholder, (1) shares owned by persons who are directors and also officers and (2) shares owned by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or
- at or subsequent to the date of the transaction, the business combination is approved by the board of directors of the corporation and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66-2/3% of the outstanding voting stock which is not owned by the interested stockholder.

Generally, a “business combination” includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the “interested stockholder” and an “interested stockholder” is a person who, together with affiliates and associates, owns or, within three years prior to the determination of interested stockholder status, did own 15% or more of a corporation’s outstanding voting stock.

We expect the existence of this provision to have an anti-takeover effect with respect to transactions our board of directors does not approve in advance. We also anticipate that Section 203 may discourage business combinations or other attempts that might result in a premium over the market price for the shares of common stock held by our stockholders. The provisions of DGCL, our amended and restated certificate of incorporation, as amended, and our amended and restated bylaws could have the effect of discouraging others from attempting

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hostile takeovers and, as a consequence, they may also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions may also have the effect of preventing changes in our management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interests.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock and each class of preferred stock is Broadridge Corporate Issuer Solutions, Inc. The transfer agent's address is 1717 Arch Street, Suite 1300, Philadelphia, Pennsylvania 19103.

Listing

Our common stock is listed on the Nasdaq Capital Market under the symbol "PSTV."

PLAN OF DISTRIBUTION

The shares of our common stock offered by this prospectus are being offered by the selling stockholder, Lincoln Park. The shares may be sold or distributed from time to time by the selling stockholder directly to one or more purchasers or through brokers, dealers, or underwriters who may act solely as agents at market prices prevailing at the time of sale, at prices related to the prevailing market prices, at negotiated prices, or at fixed prices, which may be changed. The sale of the common stock offered by this prospectus could be effected in one or more of the following methods:

- ordinary brokers' transactions;
- transactions involving cross or block trades;
- through brokers, dealers, or underwriters who may act solely as agents;
- "at the market" into an existing market for our common stock;
- in other ways not involving market makers or established business markets, including direct sales to purchasers or sales effected through agents;
- in privately negotiated transactions; or
- any combination of the foregoing.

In order to comply with the securities laws of certain states, if applicable, the shares of our common stock offered by this prospectus may be sold only through registered or licensed brokers or dealers. In addition, in certain states, the shares of our common stock offered by this prospectus may not be sold unless they have been registered or qualified for sale in the state or an exemption from the state's registration or qualification requirement is available and complied with.

Lincoln Park is an "underwriter" within the meaning of Section 2(a)(11) of the Securities Act.

Lincoln Park has informed us that it intends to use an unaffiliated broker-dealer to effectuate all sales, if any, of our common stock that it may purchase from us pursuant to the Purchase Agreement. Such sales will be made at prices and at terms then prevailing or at prices related to the then current market price. Each such unaffiliated broker-dealer will be an underwriter within the meaning of Section 2(a)(11) of the Securities Act. Lincoln Park has informed us that each such broker-dealer will receive commissions from Lincoln Park that will not exceed customary brokerage commissions.

Brokers, dealers, underwriters or agents participating in the distribution of the shares of our common stock offered by this prospectus may receive compensation in the form of commissions, discounts, or concessions from the selling stockholder and/or the purchasers, for whom the broker-dealers may act as agent. The compensation paid to any such particular broker-dealer may be less than or in excess of customary commissions. Neither we nor Lincoln Park can presently estimate the amount of compensation that any agent will receive from the selling stockholder or from any purchasers of shares of our common stock sold by Lincoln Park.

We know of no existing arrangements between Lincoln Park or any other stockholder, broker, dealer, underwriter or agent relating to the sale or distribution of the shares of our common stock offered by this prospectus.

We may from time to time file with the SEC one or more supplements to this prospectus or amendments to the registration statement of which this prospectus forms a part to amend, supplement or update information contained in this prospectus, including, if and when required under the Securities Act, to disclose certain information relating to a particular sale of shares of our common stock offered by this prospectus by the selling stockholder, including the names of any brokers, dealers, underwriters or agents participating in the distribution of such shares of our common stock by the selling stockholder, any compensation paid by Lincoln Park to any such brokers, dealers, underwriters or agents, and any other required information.

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We will pay the expenses incident to the registration, offering and sale of the shares of our common stock to Lincoln Park. We have agreed to indemnify Lincoln Park and certain other persons against certain liabilities in connection with the offering of shares of common stock offered by this prospectus, including liabilities arising under the Securities Act or, if such indemnity is unavailable, to contribute amounts required to be paid in respect of such liabilities. Lincoln Park has agreed to indemnify us against liabilities under the Securities Act that may arise from certain written information furnished to us by Lincoln Park specifically for use in this prospectus or, if such indemnity is unavailable, to contribute amounts required to be paid in respect of such liabilities.

Lincoln Park has represented to us that at no time prior to the Purchase Agreement has Lincoln Park or its agents, representatives or affiliates engaged in or effected, in any manner whatsoever, directly or indirectly, any short sale (as such term is defined in Rule 200 of Regulation SHO of the Exchange Act) of our common stock or any hedging transaction, which establishes a net short position with respect to our common stock. Lincoln Park has agreed that during the term of the Purchase Agreement, it and its agents, representatives or affiliates will not enter into or effect, directly or indirectly, any of the foregoing transactions.

We have advised Lincoln Park that it is required to comply with Regulation M promulgated under the Exchange Act. With certain exceptions, Regulation M precludes the selling stockholder, any affiliated purchasers, and any broker-dealer or other person who participates in the distribution from bidding for or purchasing, or attempting to induce any person to bid for or purchase any security which is the subject of the distribution until the entire distribution is complete. Regulation M also prohibits any bids or purchases made in order to stabilize the price of a security in connection with the distribution of that security. All of the foregoing may affect the marketability of the securities offered by this prospectus.

This offering will terminate on the earlier of (i) termination of the Purchase Agreement or (ii) the date that all shares of our common stock offered by this prospectus have been sold by Lincoln Park.

Our common stock is listed on the Nasdaq Capital Market under the symbol "PSTV".

LEGAL MATTERS

The validity of any securities offered by this prospectus will be passed upon for us by Hogan Lovells US LLP, Houston, Texas.

EXPERTS

The consolidated financial statements as of December 31, 2022 and 2021 and for the years then ended incorporated by reference in this prospectus have been so incorporated in reliance on the report of BDO USA, LLP (n/k/a BDO USA, P.C.), an independent registered public accounting firm, incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We have filed a registration statement on Form S-1 with the SEC under the Securities Act. This prospectus is part of the registration statement but the registration statement includes and incorporates by reference additional information and exhibits. We file annual, quarterly and current reports, proxy statements and other information with the SEC. The SEC also maintains a web site that contains reports, proxy and information statements and other information regarding companies, such as ours, that file documents electronically with the SEC. The website address is www.sec.gov. The information on the SEC's website is not part of this prospectus, and any references to this website or any other website are inactive textual references only.

INCORPORATION BY REFERENCE

The SEC permits us to “incorporate by reference” the information contained in documents we have filed with the SEC, which means that we can disclose important information to you by referring you to those documents rather than by including them in this prospectus. Information that is incorporated by reference is considered to be part of this prospectus and you should read it with the same care that you read this prospectus. We have filed with the SEC, and incorporate by reference in this prospectus:

- our Annual Report on Form 10-K for the year ended [December 31, 2022](#) (filed with the SEC on February 23, 2023);
- our Quarterly Reports on Form 10-Q for the quarters ended [March 31, 2023](#), [June 30, 2023](#) and [September 30, 2023](#) (filed with the SEC on April 20, 2023, August 14, 2023, and October 31, 2023, respectively);
- our Current Reports on Form 8-K filed with the SEC on [March 3, 2023](#), [April 21, 2023](#), [April 28, 2023](#), [May 16, 2023](#) and [October 31, 2023 \(reporting under Item 8.01\)](#);
- the description of our common stock contained in our Registration Statement on [Form 10/A](#) (File No. 000-32501) filed on July 16, 2001, and any amendment or report filed with the Commission for the purpose of updating the description.

We are not, however, incorporating, in each case, any documents or information that we are deemed to furnish and not file in accordance with SEC rules.

Any statement contained in any document incorporated by reference herein will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or any prospectus supplement modifies or supersedes such statement. Any statement so modified or superseded will not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of this offering, including all such documents we may file with the SEC after the date of the initial registration statement and prior to the effectiveness of the registration statement, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus and deemed to be part of this prospectus from the date of the filing of such reports and documents.

We will provide without charge to each person, including any beneficial owner, to whom this prospectus is delivered, upon written or oral request, a copy of any or all documents that are incorporated by reference into this prospectus, but not delivered with the prospectus, other than exhibits to such documents unless such exhibits are specifically incorporated by reference into the documents that this prospectus incorporates. You should direct oral or written requests by one of the following methods. Attention: Investor Relations, Plus Therapeutics, Inc., 4200 Marathon Blvd., Suite 200, Austin, TX 78756, (737) 255-7194. You may also access these documents, free of charge on the SEC’s website at www.sec.gov or on the “Investors” page of our website at www.plustherapeutics.com. The information found on our website, or that may be accessed by links on our website, is not part of this prospectus. We have included our website address solely as an inactive textual reference. Investors should not rely on any such information in deciding whether to purchase our common stock.

**DISCLOSURE OF COMMISSION POSITION ON
INDEMNIFICATION FOR SECURITIES ACT LIABILITIES**

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to our directors, officers, and controlling persons, we have been informed that in the opinion of the SEC this indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

1,300,000 Shares of Common Stock



PROSPECTUS

, 2023

PART II**Information Not Required in Prospectus****Item 13. Other Expenses of Issuance and Distribution.**

The following is a statement of estimated expenses in connection with the offering described in this registration statement. All expenses incurred with respect to the registration of the common stock will be borne by us. All amounts are estimates except the SEC registration fee.

	<u>Amount</u>
SEC Registration Fee	\$ 305
Printing Expenses	15,000
Legal Fees and Expenses	25,000
Accounting Fees and Expenses	25,000
Miscellaneous Expenses	9,695
Total	<u>\$ 75,000</u>

Item 14. Indemnification of Directors and Officers.

Section 102 of the DGCL allows a corporation to eliminate the personal liability of directors of a corporation to the corporation or its stockholders for monetary damages for breach of fiduciary duty as a director, except where the director breached the duty of loyalty, failed to act in good faith, engaged in intentional misconduct or knowingly violated a law, authorized the payment of a dividend or approved a stock repurchase in violation of the DGCL or obtained an improper personal benefit.

Section 145 of the DGCL provides, among other things, that we may indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding—other than an action by or in our right—by reason of the fact that the person is or was our director, officer, agent or employee, or is or was serving at our request as a director, officer, agent or employee of another corporation, partnership, joint venture, trust or other enterprise against expenses, including attorneys' fees, judgments, fines and amounts paid in settlement actually and reasonably incurred by the person in connection with such action, suit or proceeding. The power to indemnify applies (a) if such person is successful on the merits or otherwise in defense of any action, suit or proceeding, or (b) if such person acting in good faith and in a manner he or she reasonably believed to be in the best interest, or not opposed to the best interest, of us, and with respect to any criminal action or proceeding had no reasonable cause to believe his or her conduct was unlawful. The power to indemnify applies to actions brought by or in our right as well but only to the extent of defense expenses, including attorneys' fees but excluding amounts paid in settlement, actually and reasonably incurred and not to any satisfaction of judgment or settlement of the claim itself, and with the further limitation that in such actions no indemnification shall be made in the event of any adjudication of liability to us, unless the court believes that in light of all the circumstances indemnification should apply.

Section 174 of the DGCL provides, among other things, that a director who willfully or negligently approves of an unlawful payment of dividends or an unlawful stock repurchase or redemption may be held liable for such actions. A director who was either absent when the unlawful actions were approved or dissented at the time, may avoid liability by causing his or her dissent to such actions to be entered in the books containing minutes of the meetings of the board of directors at the time such action occurred or immediately after such absent director receives notice of the unlawful acts.

Our amended and restated certificate of incorporation, as amended, and amended and restated bylaws, filed as Exhibit 3.1 to our Annual Report on Form 10-K filed March 11, 2016 and Exhibit 3.1 to our Periodic Report on Form 8-K filed September 21, 2021, respectively, provide that we shall indemnify our directors, officers,

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employees and other agents to the fullest extent not prohibited by the DGCL or any other applicable law. In addition, we have entered into agreements to indemnify our directors and officers and expect to continue to enter into agreements to indemnify all of our directors and officers. These agreements require us, among other things, to indemnify our directors and officers against certain liabilities which may arise by reason of their status or service as directors or officers to the fullest extent not prohibited by law. These indemnification provisions and the indemnification agreements may be sufficiently broad to permit indemnification of our officers and directors for liabilities, including reimbursement of expenses incurred, arising under the Securities Act of 1933.

We maintain insurance policies under which our directors and executive officers are insured, within the limits and subject to the limitations of those policies, against certain expenses in connection with the defense of, and certain liabilities that might be imposed as a result of, actions, suits or proceedings to which they are parties by reason of being or having been directors or officers. The coverage provided by these policies may apply whether or not we would have the power to indemnify such person against such liability under the provisions of the General Corporation Law of the State of Delaware.

Item 15. Recent Sales of Unregistered Securities.

None.

Item 16. Exhibits and Financial Statement Schedules.

(a) Exhibits.

The exhibits to the registration statement are listed in the Exhibit Index to this registration statement and are incorporated herein by reference.

(b) Financial Statement Schedules.

Financial statement schedules

All schedules have been omitted because either they are not required, are not applicable or the information is otherwise set forth in the financial statements and related notes thereto.

Item 17. Undertakings.

The undersigned registrant hereby undertakes:

- (1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:
 - (i) To include any prospectus required by section 10(a)(3) of the Securities Act of 1933;
 - (ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Securities and Exchange Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and

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- (iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

provided, however, that paragraphs (a)(1)(i), (a)(1)(ii) and (a)(1)(iii) above do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Securities and Exchange Commission by the registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

- (2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
- (3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.
- (4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:
 - (A) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and
 - (B) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5) or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.
- (5) That, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
- (6) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act of 1933 and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

EXHIBIT INDEX

Exhibit No.	Exhibit Title	Filed herewith	Incorporated by Reference		
			Form	File No.	Date Filed
3.1	Composite Certificate of Incorporation		10-K	001-34375 Exhibit 3.1	03/11/2016
3.2	Certificate of Amendment to Amended and Restated Certificate of Incorporation.		8-K	001-34375 Exhibit 3.1	05/10/2016
3.3	Certificate of Amendment to Amended and Restated Certificate of Incorporation		8-K	001-34375 Exhibit 3.1	05/23/2018
3.4	Certificate of Amendment to Amended and Restated Certificate of Incorporation.		8-K	001-34375 Exhibit 3.1	07/29/2019
3.5	Certificate of Amendment to Amended and Restated Certificate of Incorporation.		8-K	001-34375 Exhibit 3.1	08/06/2019
3.6	Certificate of Amendment to Amended and Restated Certificate of Incorporation.		8-K	001-34375 Exhibit 3.1	04/28/2023
3.7	Certificate of Designation of Preferences, Rights and Limitations of Series B Convertible Preferred Stock		8-K	001-34375 Exhibit 3.1	11/28/2017
3.8	Certificate of Designation of Preferences, Rights and Limitations of Series C Convertible Preferred Stock		8-K	001-34375 Exhibit 3.1	07/25/2018
3.9	Certificate of Designation of Preferences, Rights and Limitations of Series F Convertible Preferred Stock		8-K	001-34375 Exhibit 3.1	03/03/2023
3.10	Amended and Restated Bylaws of Plus Therapeutics, Inc.		8-K	001-34375 Exhibit 3.1	09/21/2021
4.1	Description of Securities		10-K	001-34375 Exhibit 4.1	03/30/2020
4.2	Form of Common Stock Certificate		10-K	001-34375 Exhibit 4.33	03/09/2018
5.1	Opinion of Hogan Lovells US LLP	X			
10.1	Purchase Agreement between Plus Therapeutics, Inc. and Lincoln Park Capital Fund, LLC, dated August 2, 2022.		8-K	011-34375 Exhibit 10.1	08/08/2022
10.2	Registration Rights Agreement between Plus Therapeutics, Inc. and Lincoln Park Capital Fund, LLC, dated August 2, 2022.		8-K	011-34375 Exhibit 10.2	08/08/2022
10.3+	Patent and Know-How License Agreement, dated March 29, 2020, by and between Plus Therapeutics, Inc. and NanoTx, Corp.		8-K	011-34375 Exhibit 10.1	3/30/2020
10.4+	Patent & Technology License Agreement, dated December 31, 2021, between Plus Therapeutics, Inc. and the University of Texas Health Science Center at San Antonio		10-K	001-34375 Exhibit 10.2	02/24/2022

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<u>Exhibit No.</u>	<u>Exhibit Title</u>	<u>Filed herewith</u>	<u>Incorporated by Reference</u>		
			<u>Form</u>	<u>File No.</u>	<u>Date Filed</u>
10.5	<u>Distribution Agreement, dated January 14, 2022, by and among Plus Therapeutics, Inc. and Canaccord Genuity LLC</u>		8-K	011-34375 Exhibit 1.1	1/14/2022
10.6	<u>Loan and Security Agreement, dated May 29, 2015, by and between Plus Therapeutics, Inc. and Oxford Finance, LLC</u>		10-Q	001-34375 Exhibit 10.4	08/10/2015
10.7	<u>First Amendment to Loan and Security Agreement, dated September 20, 2017, by and between Plus Therapeutics, Inc. and Oxford Finance, LLC</u>		S-1/A	333-219967 Exhibit 10.45	10/03/2017
10.8	<u>Second Amendment to Loan and Security Agreement, dated June 19, 2018, by and between Plus Therapeutics, Inc. and Oxford Finance, LLC</u>		10-Q	001-34375 Exhibit 10.3	08/14/2018
10.9	<u>Third Amendment to Loan and Security Agreement, dated August 31, 2018, by and between Plus Therapeutics, Inc. and Oxford Finance, LLC</u>		S-1	333-227485 Exhibit 10.51	09/21/2018
10.10	<u>Fourth Amendment to Loan and Security Agreement dated December 31, 2018, by and between Plus Therapeutics, Inc. and Oxford Finance, LLC</u>		S-1	333-229485 Exhibit 10.52	02/01/2019
10.11	<u>Fifth Amendment to Loan and Security Agreement dated February 13, 2019, by and between Plus Therapeutics, Inc. and Oxford Finance, LLC</u>		10-K	001-34375 Exhibit 10.55	03/29/2019
10.12	<u>Sixth Amendment to Loan and Security Agreement dated March 4, 2019, by and between Plus Therapeutics, Inc. and Oxford Finance, LLC</u>		10-K	001-34375 Exhibit 10.56	03/29/2019
10.13	<u>Seventh Amendment to Loan and Security Agreement dated April 24, 2019, by and between Plus Therapeutics, Inc. and Oxford Finance, LLC</u>		10-Q	001-34375 Exhibit 10.3	05/14/2019
10.14	<u>Eighth Amendment to Loan and Security Agreement dated July 15, 2019, by and between Plus Therapeutics, Inc. and Oxford Finance, LLC</u>		10-Q	001-34375 Exhibit 10.2	08/15/2019
10.15+	<u>Ninth Amendment to Loan and Security Agreement, dated March 29, 2020 by and between Plus Therapeutics, Inc. and Oxford Finance, LLC</u>		8-K	011-34375 Exhibit 10.2	3/30/2020
10.16#	<u>Amended and Restated Employment Agreement between Marc Hedrick and Plus Therapeutics, Inc.</u>		10-Q	001-34375 Exhibit 10.6	5/16/2020
10.17#	<u>Amended and Restated Employment Agreement between Andrew Sims and Plus Therapeutics, Inc.</u>		10-Q	001-34375 Exhibit 10.7	5/16/2020
10.18#	<u>Employment Agreement between Norman LaFrance and Plus Therapeutics, Inc.</u>		8-K	001-34375 Exhibit 10.1	09/13/2021
10.19#	<u>2015 New Employee Incentive Plan</u>		8-K	001-34375 Exhibit 10.1	01/05/2016

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Exhibit No.	Exhibit Title	Filed herewith	Incorporated by Reference		
			Form	File No.	Date Filed
10.20#	First Amendment to the Plus Therapeutics, Inc. 2015 New Employee Incentive Plan, dated Jan. 26, 2017		10-K	001-34375 Exhibit 10.42	03/24/2017
10.21#	Second Amendment to the Plus Therapeutics, Inc. 2015 New Employee Incentive Plan, dated February 6, 2020		10-K	001-34375 Exhibit 10.25	03/30/2020
10.22#	Form of Notice of Grant of Stock Option under the 2015 New Employee Incentive Plan		S-8	333-210211 Exhibit 99.5	03/15/2016
10.23#	Form of Stock Option Agreement under the 2015 New Employee Incentive Plan		S-8	333-210211 Exhibit 99.4	03/15/2016
10.24#	Form of Notice of Grant and Stock Option Agreement under the 2020 Stock Incentive Plan.		10-K	001-34375 Exhibit 10.26	02/24/2022
10.25#	2020 Stock Incentive Plan (as further amended and restated)		8-K	001-34375 Exhibit 10.1	04/21/2023
10.26+	Master Services Agreement between Piramal Pharma Solutions, Inc. and Plus Therapeutics, Inc.		10-K	001-334275 Exhibit 10.24	02/22/2021
10.27#	Form Indemnification Agreement		8-K	001-34375 Exhibit 10.1	02/06/2020
10.28	Subscription and Investment Representation Agreement, dated March 3, 2023, by and between Plus Therapeutics, Inc. and the purchaser signatory thereto		8-K	001-34375 Exhibit 10.1	03/03/2023
23.1	Consent of BDO USA, P.C., Independent Registered Public Accounting Firm	X			
23.2	Consent of Hogan Lovells US LLP (included in Exhibit 5.1)	X			
24.1	Power of Attorney (see signature page)	X			
107	Fee Table	X			

Indicates management contract or compensatory plan or arrangement.

+ Portions of this exhibit have been excluded pursuant to Item 601(b)(1)(iv).

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the Registrant has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Austin, State of Texas, on November 14, 2023.

PLUS THERAPEUTICS, INC.

By: /s/ Marc H. Hedrick, MD
Marc H. Hedrick, MD
President and Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints Marc H. Hedrick, MD and Andrew Sims, and each of them, his or her true and lawful attorneys-in-fact and agents, with full power of substitution and re-substitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments, including post-effective amendments, to this Registration Statement, and any registration statement relating to the offering covered by this Registration Statement and filed pursuant to Rule 462(b) under the Securities Act of 1933, and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done, as fully for all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that each of said attorneys in fact and agents or their substitute or substitutes may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

<u>Name</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Marc H. Hedrick, MD</u> Marc H. Hedrick, MD	President and Chief Executive Officer and Director <i>(Principal Executive Officer)</i>	November 14, 2023
<u>/s/ Andrew Sims</u> Andrew Sims	Chief Financial Officer <i>(Principal Financial Officer and Principal Accounting Officer)</i>	November 14, 2023
<u>/s/ Richard J. Hawkins</u> Richard J. Hawkins	Chairman of the Board	November 14, 2023
<u>/s/ Howard Clowes</u> Howard Clowes	Director	November 14, 2023
<u>/s/ An van Es-Johansson, MD</u> An van Es-Johansson, MD	Director	November 14, 2023
<u>/s/ Robert Lenk, Ph.D.</u> Robert Lenk, Ph.D.	Director	November 14, 2023
<u>/s/ Greg Petersen</u> Greg Petersen	Director	November 14, 2023



Hogan Lovells US LLP
609 Main Street, Suite 4200
Houston, TX 77002
T +1 713 632 1400
F +1 713 632 1401
www.hoganlovells.com

November 14, 2023

Board of Directors
Plus Therapeutics, Inc.
4200 Marathon Blvd., Suite 200
Austin, TX 78756

To the addressee referred to above:

We are acting as counsel to Plus Therapeutics, Inc., a Delaware corporation (the “**Company**”), in connection with its registration statement on Form S-1, as amended (the “**Registration Statement**”), filed with the Securities and Exchange Commission under the Securities Act of 1933, as amended (the “**Act**”) relating to the resale of up to 1,300,000 shares of the common stock, par value \$0.001 per share (the “**Common Stock**”) of the Company (the “**Shares**”), which are reserved for future issuance pursuant to that certain Purchase Agreement between the Company and Lincoln Park Capital Fund, LLC, dated as of August 2, 2022 (the “**Purchase Agreement**”). This opinion letter is furnished to you at your request to enable you to fulfill the requirements of Item 601(b)(5) of Regulation S-K, 17 C.F.R. § 229.601(b)(5), in connection with the Registration Statement.

For purposes of this opinion letter, we have examined copies of such agreements, instruments and documents as we have deemed an appropriate basis on which to render the opinions hereinafter expressed. In our examination of the aforesaid documents, we have assumed the genuineness of all signatures, the legal capacity of all natural persons, the accuracy and completeness of all documents submitted to us, the authenticity of all original documents, and the conformity to authentic original documents of all documents submitted to us as copies (including pdfs). As to all matters of fact, we have relied on the representations and statements of fact made in the documents so reviewed, and we have not independently established the facts so relied on. This opinion letter is given, and all statements herein are made, in the context of the foregoing.

This opinion letter is based as to matters of law solely on the Delaware General Corporation Law, as amended. We express no opinion herein as to any other statutes, rules or regulations.

Based upon, subject to and limited by the foregoing, and assuming that no Shares will be sold at a price which is less than the Floor Price (as defined in the Purchase Agreement), we are of the opinion that following (a) effectiveness of the Registration Statement, (b) issuance of the Shares pursuant to the terms of the Purchase Agreement and in accordance with the resolutions of the Company’s Board of Directors, and (c) receipt by the Company of the consideration for the Shares specified in the Purchase Agreement, the Shares will be validly issued, fully paid, and nonassessable. This opinion letter has been prepared for use in connection with the Registration Statement. We assume no obligation to advise of any changes in the foregoing subsequent to the effective date of the Registration Statement.

We hereby consent to the filing of this opinion letter as Exhibit 5.01 to the Registration Statement and to the reference to this firm under the caption “Legal Matters” in the prospectus constituting a part of the Registration Statement. In giving this consent, we do not thereby admit that we are an “expert” within the meaning of the Act.

Very truly yours,

/s/ Hogan Lovells US LLP

HOGAN LOVELLS US LLP

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

Plus Therapeutics, Inc.
Austin, Texas

We hereby consent to the incorporation by reference in the Prospectus constituting a part of this Registration Statement of our report dated February 23, 2023, relating to the financial statements of Plus Therapeutics, Inc. (the “Company”) appearing in the Company’s Annual Report on Form 10-K for the year ended December 31, 2022.

We also consent to the reference to us under the caption “Experts” in the Prospectus.

/s/ BDO USA, P.C.

Austin, Texas

November 14, 2023

Calculation of Filing Fee Tables

Form S-1
(Form Type)

Plus Therapeutics, Inc.
(Exact Name of Registrant as Specified in its Charter)

Table 1: Newly Registered and Carry Forward Securities

	Security Type	Security Class Title	Fee Calculation or Carry Forward Rule	Amount Registered (1)	Proposed Maximum Offering Price Per Unit (2)	Maximum Aggregate Offering Price	Fee Rate	Amount of Registration Fee
Fees to Be Paid	Equity	Common Stock, \$0.001 par value per share	457(c)	1,300,000	\$1.59	\$2,067,000.00	0.0001476	\$305.09
	Total Offering Amounts					\$2,067,000.00	0.0001476	\$305.09
	Total Fees Previously Paid							—
	Total Fee Offsets							—
	Net Fee Due							\$305.09

(1) Represents the 1,300,000 shares of common stock that are issuable pursuant to a purchase agreement with the selling shareholder named herein. Pursuant to Rule 416(a) under the Securities Act of 1933, as amended, the registrant is also registering hereunder an indeterminate number of shares that may be issued and resold resulting from stock splits, stock dividends or similar transactions.

(2) Based on the closing price of shares of the registrant's common stock on November 8, 2023.